VOLUME 12 NUMBER 4

Food-Drug-Cosmetic Law Journal

AUGUST • 1957

Papers Delivered at The Joint Conference of The Food Law Institute of the United States and Scientific Organizations in Great Britain (Food Group of the Society of Chemical Industry; Society for Analytical Chemistry; and Association of Public Analysts) on Chemical Additives in Food, in London, England, on July 26, 1957

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A COMMERCE CLEARING HOUSE PUBLICATION

PUBLISHED IN ASSOCIATION WITH THE FOOD LAW INSTITUTE, INC.

The editorial policy of this JOURNAL is to record the progress of the law in the field of food, drugs and cosmetics, and to provide a constructive discussion of it, according to the highest professional standards. The FOOD DRUG COSMETIC LAW JOURNAL is the only forum for current discussion of such law and it renders an important public service, for it is an invaluable means (1) to create a better knowledge and understanding of food, drug and cosmetic law, (2) to promote its due operation and development and thus (3) to effectuate its great remedial purposes. In short: While this law receives normal legal, administrative and judicial consideration, there remains a basic need for its appropriate study as a fundamental law of the land; the JOURNAL is designed to satisfy that need. The editorial policy also is to allow frank discussion of food-drug-cosmetic issues. On this basis, contributions and comments are invited.

The FOOD DRUG COSMETIC LAW JOURNAL is published monthly by Commerce Clearing House, Inc. Subscription price: $15 per year, including a handsome binder to hold one year's issues. Single copies are $1.50 each. Editorial and business offices, 4025 W. Peterson Ave., Chicago 30, Ill. Printed in United States of America.

August, 1957
Volume 12 • Number 8

Entered as second-class matter December 30, 1948, at the Post Office at Chicago, Illinois, under the Act of March 3, 1879.

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REPORTS

TO THE READER

Meeting of Food and Drug Men

Program.—The official program of an important international meeting held recently in London, England, is reproduced—in substance—below. The conference met in morning and afternoon sessions, beginning at 10 o'clock and 2:30 o'clock, respectively. Speakers are listed in the order of their appearance.

"Conference on CONTROL OF CHEMICAL ADDITIVES IN FOOD"

(A Joint Meeting of The Food Law Institute of the United States, the Food Group of the Society of Chemical Industry, the Society for Analytical Chemistry, and the Association of Public Analysts, of Great Britain, Held at the Royal Institution, London, on July 26, 1957)

Morning Session

"The Control of Chemical Additives in Food, Other Than Antibiotics"

Chairman: Mr. Charles Wesley Dunn, President of The Food Law Institute

Introduction of chairman by Dr. J. H. Hamence, President of the Society for Analytical Chemistry

Chairman's opening remarks

Addresses by:

Mr. George P. Larrick, Commissioner of Food and Drugs, United States Department of Health, Education, and Welfare, and Dr. A. J. Lehman, Director of Pharmacology, United States Food and Drug Administration

Dr. C. A. Morrell, Director, Food and Drug Directorate, Canadian Department of National Health and Welfare

Dr. N. C. Wright, C. B., Chief Scientific Adviser (Food) to the British Ministry of Agriculture, Fisheries and Food

Dr. E. J. Miller, Chemist in Plant Pathology Laboratory, British Ministry of Agriculture, Fisheries and Food

Discussion

Afternoon Session

"The Control of Chemical Additives in Food with Special Reference to Antibiotics"

Chairman: Sir Harry Jephcott, Chairman of the Council of Department of Scientific and Industrial Research

Chairman's opening remarks

Addresses by:

Dr. Henry Welch, Director, Division of Antibiotics, United States Food and Drug Administration

Dr. C. A. Morrell and Dr. F. S. Thatcher, Chief, Microbiology Laboratory, Food and Drug Directorate, Canadian Department of National Health and Welfare

Mr. A. L. Bacharach, Chairman, *Sous-Commission* on Antibiotics in Food appointed by *Commission Interationale des Industries Agricoles* and the *Bureau International Permanent de Chimie Analytique*

Discussion

(Editor's Note: The papers read at both sessions of the conference are published in full text in this August JOURNAL. Transcripts of the floor discussions appear below.)

Conference Floor Discussion—Morning Session.—A verbatim transcript of the floor discussion following the morning session of the conference follows:

"Chairman: Mr. Charles Wesley Dunn

"The CHAIRMAN: Ladies and gentlemen, we have exactly 30 minutes for our informal discussion, and therefore it is necessary to ask that each questioner shall be very brief, and that he should address the question to one of the four speakers this morning.

"The first speaker from the floor is Mr. George Taylor, a Past President of the Society of Analytical Chemistry and a Past President of the Association of Public Analysts.

"Each speaker will be allowed 5 minutes.

"Mr. George TAYLOR: Mr. Chairman, I am very greatly honoured by this invitation to open the discussion. This morning we have been privileged to have the opportunity of hearing four authoritative addresses on the subject of the control of additives in food. I doubt whether there is now in this room anybody present who does not appreciate the importance of the subject. All aspects of that subject were considered, but I think there is one aspect which has been a little lightheartedly treated. In fact, sir, I am not quite sure that it is not wishful thinking.

"With the exception of Dr. Miller the question of enforcement has not been gone into very thoroughly. It is a fact, I think, that enforcement is in matters such as food additives dependent entirely upon reliable and accurate methods of analysis. It is also a fact that modern technology has advanced and is advancing so fast that always chemical analysis is one step behind production, therefore the problem to the analyst is an extremely big one. I think it is one that should, as was referred to in the opening of this meeting, be a matter of as much collaboration as possible between industry and the analysts.

"There is therefore one question, sir, that I would like to ask. In England here, obviously the control of additives would be administered by the Food and Drugs Act. The Food and Drugs Act is administered through food authorities—food and drug authorities—and they are constituted by County Councils, Borough Councils, Municipal Councils and, indeed, the Urban District Council with a population of over 40,000 which may wish to become a food authority. That is to say, it is decentralised, as I understand it. However, the position in America is that these food additives come also under the Food, Drug and Cosmetics Act which is administered first by the Secretary of the Health Department and then through the Food and Drugs administration. That, I take it, is an autonomous body working down through commissioners, divisional executive officers and so on, to field stations. It is in those field stations that the sampling and analytical work is done, but that system is a centralised system. In England it is decentralised. It is common practice now—and Dr. Miller has shown us recently that in England it is advancing fast—to have conferences between Government departments and manufacturers on the question of these products, and on the table will be laid at those meetings, without any doubt, by all reputable manufacturers full details of the composition, physiological properties and analytical methods involved in those products.

"Is it the case that in the United States of America, with their centralised system, the analyst at the bottom end of the chain is given at a very early date full information about all the properties and the analytical requirements of any new products? If so, that is a kind of co-operation which I think is necessary nowadays in order to enable this control of additives to food to be achieved.

"Mr. John L. HARVEY: The gentleman is entirely correct in his description of the procedure followed in the United States and, of course, the uniformity of method and the autonomy is particularly necessary.

"We do have, of course, 48 States, and several territories have independent food and drug enforcement organisations of their own. However, the purpose there is primarily, through the association of official agricultural chemists and others, to provide the organisations of the individual States with the same methods and analytical data that we possess in the central organisation.

"I might say that one of the problems, as the gentleman states, is that in effect the analyst is so often always one step behind the production. One of the contemplations of the scheme now being debated as a legislative proposal in the United States is an idea that as part of the prior approval of the use of a particular additive—and that is now true of the already effective pesticidal law—satisfactory, not necessarily perfect, methods for the detection and quantitative evaluation of residues in food products must be on hand before the approval of the use of the substance, and if that can be done on a voluntary basis, we have tremendous problems, but we avoid to a large extent the chemist being behind production, and so on.

"The CHAIRMAN: May I be permitted to add two comments to what Mr. Harvey has said? He has not stated what I will now say, which is that the United States Food and Drug Administration in the estimation of the food industry of our country is doing a magnificent enforcement and administrative job. We have great confidence in it. We have great respect for it, and we have a centralised Federal enforcement that is very severe indeed, but it is also a very constructive one. To answer the question, sir, one of the constructive measures which the F. D. A. has incorporated is to have scientific conferences in Washington, where the F. D. A. brings together the scientists of the industry and outside of industry to discuss these major questions of major analysis or whatever it may be, in order to determine the very thing that you have advocated—general information as to common procedure in order to comply fully with the Act.

"Secondly, the F. D. A. has recently agreed to have a conference with the leaders of our food industry in November, when they will present to us their problems and we, through the industry, will discuss with them the solution of their problems in an entirely constructive and co-operative way. We hope through this conference to create a permanent watch-dog committee, if we may call it such, which shall be a permanent body to keep in touch with the F. D. A. and help it to solve our problems.

"We do not like, in our country, an arbitrary government, and we believe in a democratic government of co-operation, but strict enforcement of the tenets of the law by the government, and so our policy is to co-operate in the industry as fully as possible, industrially and scientifically, with the F. D. A. and thus bring about the greatest degree of voluntary compliance with the law. That is our objective. We have to prosecute the industrial violaters with the greatest severity, but the legitimate manufacturers have the objective of having a voluntary co-operation on an educational basis, and we want to know what the F. D. A. think, and we tell them what we think. In this way we will have a common basis for procedure to secure the full purpose of the Act, which is to protect the public health, and protect the industry.

"Our second speaker from the floor is Mr. R. S. Link, B.Sc., who is from Bowaters Research and Development Company.

"Mr. R. S. LINK, B.Sc.: Mr. Chairman, there is just one aspect that I

would like to touch upon quite briefly, and that is the fact that whereas we are concerned today with the addition of chemicals to foodstuffs, we should really also have at the back of our minds the problem which poses itself by the coincidental introduction of chemicals into foodstuffs which are not properly added to the foodstuffs themselves, or to the foodstuffs at the time the crops are raised, or while the foodstuffs are being preserved, but when the foodstuffs are being packaged.

"This is an extremely important subject nowadays when so many new packages have come onto the market in the shape of all makes of papers, wrappers and plastic materials, and I am well aware that many Government subcommittees have given serious thought to the problem of plasticisers, for instance, in foodstuff packaging films, and such matters.

"I think it should be a matter that must command our attention to a degree hardly less than the addition of chemicals to foodstuffs proper—namely, the coincident introduction by contact of packaging materials of chemicals which may have a deleterious effect.

"The CHAIRMAN: The answer to that question is very brief and complete, and that is that the new amendment under which it falls upon the F. D. A. to control chemical additives in food reaches the migratory addition of chemicals from containers of foods, which is the point that you made.

"Is there any additional comment, Mr. Harvey, that you would like to make to this?

"Mr. John L. HARVEY: I believe the language is 'a substance that directly or indirectly under the intended conditions of use becomes a component to food.' That is to say, if it is a foreseeable hazard; obviously we cannot devise a method requiring prior approval of an accident.

"The CHAIRMAN: The only provision of the Act now that deals with the accidental contamination of food is the Miller amendment, controlling the pesticides in foods.

"The next speaker from the floor is Professor A. C. Frazer.

"Professor A. C. FRAZER: Mr. Chairman, ladies and gentlemen, we have had a very clear and delightful exposition on these problems this morning, and although I have attended a great many meetings about chemical additives in food I cannot ever recall one when I ended the morning being in substantial agreement with everything said.

"The three points I would like to raise I think might be commented on by any of this morning's speakers. The first is on the question of tests. I think that a great deal of our problem on this question of what tests and how much should be done comes from the fact that so many people who make suggestions in this field have never done these tests, and have no intention of doing them. I would like to see consideration of this matter rather largely confined to people who have actual experience in this field, who are not going to make suggestions which involve the use of hundreds and thousands of animals and other things which are really quite impracticable.

"What is perhaps in line with this, I had the privilege recently of sitting on a W. H. O. panel on this subject. I cannot of course reveal what the results were because they are still under consideration, but we did, I think I can say, come to a fairly substantial agreement on this rather difficult subject. Largely I think that was because most, if not all, of us had had practical experience in this field.

"The second point about tests that I should like to make is that it does seem to me that there is a need for more research in this field, particularly on methods to find out which are the methods which we can in fact usefuly discard, because they do not really justify their existence on economic grounds.

(Continued on page 514)

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Chemical Food Additives

By GEORGE P. LARRICK and ARNOLD J. LEHMAN, M. D.

This Paper, Read at the Morning Session, Conference of FLI and British Scientific Societies, Suggests General Requirements to Be Met Before a New Food Additive Is Used Commercially

THE PRODUCTION and handling of food has undergone a revolution within the past generation in many countries. When the first food and drug law was being considered in the United States, around 1900, some chemical additives used in food were a hazard to the public health. Poisonous preservatives and poisonous coloring materials were being used. Therefore, the original law—enacted in 1906—declared that food would be adulterated if "it contains any added poisonous or other added deleterious ingredient which may render such article injurious to health." Under that law, each food was considered alone; if it did not contain sufficient added poison to render it injurious, no action could be taken. But the total intake of poison by the consumer could not be controlled on a single-product basis. If each of three items of food had contained one third of the amount of poison required to make it harmful, each would have been legal under the 1906 law, but the consumer who was unfortunate enough to eat these three items at a single meal might have been injured.

In 1938, a new law—the Federal Food, Drug, and Cosmetic Act—was passed in the United States. It attempted to remedy the defect in the earlier law by forbidding the addition of any poisonous or

deleterious substance to any food except where it is required or cannot be avoided. When such substance is required or cannot be avoided, the government shall establish, by regulation, the quantity that may be present without hazard to the public health.

This doesn't solve the problem. It forbids the addition to food of any substance known to be poisonous or deleterious, leaving uncontrolled the addition of chemicals that have not been tested enough to show whether they are poisonous.

The present law permits untested or inadequately tested chemicals to enter the food supply. If the manufacturer who chooses to use new chemicals decides that he does not care to conduct adequate toxicity tests, the burden of determining whether the new chemical should be in food then falls upon someone else. If our government had the facilities and conducted the tests, the law still would permit untested materials to be used in food during the time they are under investigation.

Tremendous strides were made in the development of new chemicals during and following World War II. Since 1945, an amazing number of products have been suggested for possible use in foods and it is evident that better procedures for safeguarding the public health are necessary. The situation was brought to public attention in the United States in 1950, 1951 and 1952 by a select committee of the House of Representatives that investigated chemical additives in the food supply. This committee decided that new legislation is necessary, and recommended its enactment. Since then a number of proposed laws have been before the Congress of the United States; at present, there are several proposals before the Congress for consideration.

Mr. Larrick, Who Is the United States Commissioner of Food and Drugs, Has Held That Position Since 1954. He Has Been a Career Employee, Food and Drug Administration, for Almost 35 Years

Dr. Lehman Directs the Division of Pharmacology, FDA. Before Joining the Administration, He Headed the Pharmacology Department, University of North Carolina School of Medicine

We believe the following general requirements should be met before a new food additive is used commercially:

The additive should be tested thoroughly to show what effect it produces in treated food, and what residues remain from the additive, or reaction products resulting from its use. Feeding tests on animals should show that exaggerated use of the additive produces no harmful effects or, if it does, they should show at what level of use it produces no harmful effect. The results of the tests should be submitted to the government, and the proposed use of the additive should not be allowed until the government agrees that it is safe and so indicates by issuing an appropriate order.

On Definition of Terms

The terms "food additive" and "chemical additive" should be defined broadly to include any substance the intended use of which results or may result, directly or indirectly, in its becoming a component, or otherwise affecting the characteristics, of any food. To avoid the necessity for elaborate testing of common chemicals, such as table salt, substances generally recognized by appropriate experts as safe could be exempted from the definition.

There should be adequate safeguards against arbitrary or capricious government decisions.

Awareness of the chemical food-additive problem is increasing in many parts of the world. The very fact that this meeting is being held here in London and is being attended by representatives from a number of countries indicates the world-wide awareness of the need for new procedures to regulate the increasing use of new chemicals. This is gratifying.

One question which we are continually meeting in the United States is: "Why is it necessary to have the new chemical additives in food?" No doubt the answer is apparent to all attending this meeting. An adequate supply of good food is necessary to a healthy nation and a good economy. The progress of nations through the centuries has been closely linked to the adequacy and the wholesomeness of their food supply. There are nations in the world today that are in serious plight because their people exist on a dietary intake that is insufficient or because of periodic famines.

Certainly, any steps that can be taken to insure a greater supply of good food to the undernourished would improve the well-being of the world. Increased amounts of good food are frequently made possible by the safe use of chemical additives. Moreover, those countries of the world that have adequate food have in the past generation been able to obtain a greatly diversified supply of food from all parts of the world with the help of additives. Their diet is more attractive; their people are better nourished. This leads to improvement in their health as well as improvement in the economic status of the faraway countries which supply the new foodstuffs—yet the transportation of foods from one corner of the earth to another frequently requires food additives.

The United States economy is being geared more and more to the employment of women in industry and business. Today, approximately 22 million women are employed outside the home in our country; the reason that many of them can be so employed is that they have convenience foods available that can be made ready for the table quickly. Many of these convenience foods would not be possible without the chemicals that are being incorporated in the food today.

Therefore, whether our object is to reduce starvation, to increase the variety of attractive foods or to release women from the drudgery of the kitchen, we are faced with the need for chemical additives in food-handling and -processing today.

This brings problems that will not be completely solved by the passage of new laws. The paper which has been prepared by Dr. Henry Welch of the Food and Drug Administration will discuss some of the problems arising from uses of antibiotics. Among other things, drug uses of the antibiotics in dairy herds in the United States have resulted in the addition of penicillin to the milk supply in quantities that could be a hazard to the health of individuals very sensitive to the drug. Another problem arises from the appearance of pesticide

chemicals in the milk supply of the country. Pesticides are being employed today so that minute residues are occurring in market milk. The peculiar place that milk has in the diet of infants and many invalids requires unusual precautions to keep it free from poisonous materials. We do not have the final answer here, but the matter is under active consideration.

Antibiotics have been proposed as additives to preserve food. We do not know enough yet about the effect of long-term consumption by man of significant quantities of antibiotics to sanction their widespread addition to the food supply. We have established tolerances for two antibiotics in uncooked poultry because poultry is always cooked before it is eaten and because the evidence in our possession shows that no significant residue remains in the cooked meat when the amount of antibiotic in uncooked poultry is within the tolerance level.

Special Question of Coal-Tar Colors

The coal-tar colors are causing concern. Soon after our 1938 law was passed, we established—as authorized by the law—a list of coal-tar colors which, according to the best scientific evidence then available, were absolutely harmless. In the years that followed, the science of pharmacology made great progress. When improved techniques were applied to these materials, they showed that some of the colors formerly considered harmless could produce adverse effects when fed to test animals in relatively high dosage. These colors may not be harmful when used in an ordinary concentration in food, but they certainly do not meet the requirement of the law that they must be "harmless." We have therefore removed two orange colors and a red color from the list eligible for certification for internal consumption and we are in the process of removing four yellows.

Some people have misinterpreted this action. They have charged that the coal-tar colors are capable of causing cancer because one of the intermediates used in the manufacture of some of the food dyes is recognized as capable of causing cancer. We do not know of any evidence that any coal-tar color now permitted in food, or any of the three colors recently removed from the list of permitted colors, is capable of causing cancer when added to man's food supply. We do not agree that chemicals made from a harmful starting material must themselves be harmful.

There is considerable public concern about cancer-producing substances. Last August in Rome, Italy, there was an international con-

ference on cancer. Some of the comments made there to and for scientists were reported by the press and publicized widely in our country. They were interpreted as indicating that many cancer-producing materials are being added to the food supply.

There have been some suggestions, as a result, that an additive should not be allowed in food if it produces any cancer in any test animal by any route of administration. Before concluding that this would be wise, we should consider its implications. Cancers can be produced in test animals by repeated injection of sugar solution into muscle tissue—or injection of peanut oil or cottonseed oil or lard or tannic acid. Probably, repeated injections of some other common food chemicals will produce cancer. Do these results, obtained by procedures never employed at the dining table, mean that sugar, vegetable oils, or coffee and tea, which contain tannic acid, should be taken out of the food supply?

Certainly, we do not suggest the addition to food of any new chemical until reliable tests have shown beyond a reasonable doubt that it does not produce cancer or other disorders when eaten. But we think it unwise to become so possessed of a cancer phobia that we lose perspective.

This raises the question: "How much animal testing is needed to show the safety of a new chemical?" It seems evident that adequate testing of a chemical that may be present in food eaten by man for a lifetime requires studies in which the material is fed to a test animal, such as the rat, for its lifetime. The test should include observations on food consumption, effects on ration digestibility and utilization, growth, absorption, excretion and tissue storage of the additive, mortality, organ weights, blood changes, blood and urine chemistry, observable changes in behavior of the animal or the functions of any organ system, effects on reproduction and lactation. Microscopic examination of the animal's tissues after death is important.

These studies should be supplemented by another feeding test on another animal, such as the dog, to detect species differences. A one-year test with the second species may suffice if the results of both tests are favorable. But no simple rigid program can be laid down that will give all the answers about the safety of each new additive in all its possible applications. An additive may be altered when incorporated in food or it may react with constituents of the food. The changed additive or the reaction product may have different

toxicity. We must remember that normal food constituents or other substances added to food may have a similar pharmacological action or may accentuate the toxic action of the additive. The influence of the additive upon the nutritionally important constituents of food and its effect on the stability of nutrients in food must be considered.

We have made no effort here to state all of the tests that may be required or to explore the difficult problems of interpreting pharmacological data and translating animal-test results into permissible human-use levels that have adequate safety margins. It is evident that a generous safety factor must be present when results of toxicity studies on lower animals are relied upon to determine at what level a chemical may be fed without hazard to man.

There are a number of authoritative writings on this problem. The Expert Committee on Food Additives of the Joint Foreign Agriculture Organization-World Health Organization of the United Nations issued its *General Principles Governing the Use of Food Additives* in December, 1956. The opinions of eminent scientists of the world, as set forth in this document, are very useful. Also, we have relied on very similar principles contained in a statement "Principles and Procedures for Evaluating the Safety of Intentional Chemical Additives in Foods" issued in November, 1954, by the Food Protection Committee, Food and Nutrition Board, National Research Council, in our country.

After a proposed chemical-additive use has been shown to be safe by the best procedures available to man, we believe the additive should be allowed in food only if it serves a useful purpose. No available procedure will give absolute assurance that food containing an added chemical is completely safe for all men under all conditions. We can determine beyond a reasonable doubt that a proposed use is safe, but we see no need to tolerate even any very slight residual risk unless the additive does serve a useful purpose.

Chemical food additives have a very helpful and very necessary place in the world today. They are here to stay. We must learn how to use them safely. The minimum control would appear to be a procedure that requires adequate testing of a chemical before it is employed commercially in food. The test results should be submitted to the government, and the chemical should not be used until the government—acting for all the people—agrees that it is safe for the proposed use. **[The End]**

BY HENRY WELCH

Control of Antibiotics in

THE EXTENSION of the uses of antibiotics to fields other than prophylaxis and therapy of human disease has magnified the problems of the United States Food and Drug Administration from the standpoint of side reactions and their possible public-health significance. Antibiotics are used in animal nutrition for promotion of growth in swine, chicks and poults. Therapeutic and prophylactic use of antibiotics is made in animals such as cows, beef cattle, swine, chicks and mink. These drugs are now being used as crop sprays to prevent blight in apples, pears, walnuts and beans, and bacterial disease of tobacco, tomatoes, peppers, cherries, and others. Studies have been made to show the value of antibiotics in the preservation of vegetables, fish, beef, ham and other perishables.

Food Animals—Growth Stimulation and Product Preservation

Antibiotics used for growth stimulation are usually present in feed in small amounts (five to 20 parts per million (p. p. m.)). When used in these quantities, the drug is not found in the blood or tissue of the animal. Where 50-200 p. p. m. are used for prophylactic or therapeutic purposes in chicks or poults, residues may be demonstrated while the animal is being fed these high concentrations. However, the antibiotics are excreted within a few days after the drug is withdrawn. The use of antibiotics as described above, under normal marketing conditions, does not—in our opinion—constitute a public-health hazard. As used on crops in the United States, the antibiotics are dissipated before the edible portion of the plant is formed; since they do not reach the consumer, no public-health problem is involved.

Extensive experimental research has been conducted to explore the potentialities of antibiotics as food preservatives. In November,

tics in Food

Dr. Welch's Paper—Read at the Afternoon Session, July 26 Conference in London, England—Discussed Effects, on Food for Humans, of Antibiotics Used in Animal Feeds and Drugs. He is Director of the Division of Antibiotics, United States Food and Drug Administration

1955, the Food and Drug Administration approved the use of chlortetracycline in the preservation of raw poultry. The tolerance for this drug was granted under the provisions of the Miller Pesticide Chemicals Amendment to the Federal Food, Drug, and Cosmetic Act, passed by the Eighty-third Congress in 1954. The drug acts as a preservative and extends the shelf life of the fowl. Under the Miller Amendment, the application demonstrated "usefulness" to the satisfaction of the Department of Agriculture and "safety" to that of the Food and Drug Administration.

In the actual processing, the cleaned, eviscerated birds are added to a tank about one-third full of water containing 10-30 p. p. m. of antibiotic. The tank is then filled to the top with chipped ice. The proportion is usually one third antibiotic water, one third birds and one third ice. Air hoses are placed in the bottom of the tank and the whole vigorously agitated. This process goes on for one-half hour to two hours, at which time the birds are removed and prepared for shipment. The tolerance in the raw bird for the chemical was established at seven parts per million in any portion of the bird. Before this tolerance was granted, it had to be shown that no significant residue of the antibiotic could be found in the bird after cooking by broiling, frying, boiling or baking. It is thus apparent that no active residue is contained in the product as consumed, since fowl are not eaten in the raw state.

A considerable number of investigative studies of the usefulness of antibiotics in the preservation of fish and meats has also been completed. However, approval of such by the establishment of tolerances under the Miller Amendment can be obtained only when conclusive

evidence is presented that this proposed use is not detrimental to the health of the general public.

The actual or potential introduction of antibiotics into the food supply poses the same problem as does the use of any other chemical, and this growing use of chemicals in food is one of the most serious problems facing the Food and Drug Administration at this time. It should be emphasized that the problem of contamination of foods with antibiotics is now a small one when compared to our other food safety problems. There is virtually no limit to the expanding list of chemicals that may find their way into our food supply. They are promoted as stabilizers, preservatives, disinfectants, antioxidants, extenders, tenderizers, emulsifiers, growth promoters, fumigants, herbicides, defoliants, fungicides, miticides, bleaches, sweeteners, conditioners, colors and flavors. Food packages which incorporate new plastics, enamels, films, plasticizers, catalysts and coatings are further potential sources of food contamination.

Indirect Introduction into Food Supply

In addition to the planned introduction of antibiotics into the food supply, these drugs also may find their way into foods indirectly. In 1948 it was first noted that when milk from cows treated for mastitis by intramammary infusion was mixed with antibiotic-free milk for the purpose of making cheese, failure to produce a satisfactory cheese product often resulted. This was due to the inhibition of the starter culture used in cheese manufacture by the antibiotic present in the milk. Realizing that antibiotics might also reach the consumer via the milk, the Food and Drug Administration by regulation required that mastitis preparations carry a warning in their labeling to the effect that "milk from treated segments of udders should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment." In further recognition of the possibility that antibiotics might get into the food supply, a statement of policy was issued in February, 1953, by the Secretary of the Department of Health, Education, and Welfare, concerning the direct or indirect addition of antibiotic drugs to foods for human consumption. In effect, the policy statement was as follows:

> The presence of antibiotic drugs in foods intended for human consumption, or the direct or indirect addition of such drugs to such foods, may be deemed an adulteration within the meaning of section 402 of the Federal Food, Drug, and Cosmetic Act.

Very large amounts of antibiotics are used in the treatment of milk-producing cows with mastitis. It is estimated that more than 75 tons of these drugs are used yearly in the treatment of this widespread infection. Most infected cows are treated by udder infusion, and a variety of products are available for this purpose. Penicillin is used perhaps more frequently than other antibiotics, since this drug is quite effective in cases caused by streptococci, particularly *Streptococcus agalactiae*, the organisms responsible for most cases of mastitis. However, the disease is caused by other organisms, such as the corynebacteria and the coli-aerogenes group of organisms; as a result, other antibiotics such as dihydrostreptomycin, streptomycin, the tetracyclines, neomycin, bacitracin and the sulfonamides are used for treatment and prophylaxis.

Average Amounts of Drugs Used in Treatments

Treatment usually consists of a single tubeful or syringeful of the preparation for each infected quarter, but as many as four treatments at 12-hour intervals may be necessary per quarter. Thus, with a single treatment, an animal treated with a combination preparation may be administered 500,000 units of penicillin, 500 mg. of dihydrostreptomycin, 50 mg. of neomycin and 750 mg. each of sulfanilamide and sulfathiazole. If the infection is severe, the animal may receive as much as four times these amounts within a 48-hour period.

When the antibiotic preparation used is effective, the clinical result is quite dramatic and a marked change in the appearance of the teat and udder takes place within 24 hours. However, the disappearance of the signs of infection and consequent reduction in inflammation is no guarantee the infection is eliminated. This can only be determined by bacteriologic examination of the milk. Certainly a favorable change in appearance of the infected quarter is no guarantee that the drugs infused have been completely absorbed or eliminated. As a matter of fact, experimental evidence points to the contrary. It is necessary to milk infected cows twice daily for a period of at least three days to be sure that the great bulk of the drugs has been milked out. Experience has shown that substantially the entire amount of infused antibiotic is eliminated by such regular milking. It appears that failure to follow the caution in the labeling of mastitis preparations concerning discarding milk from treated cows is largely responsible for antibiotic residues in the milk supply.

Results of Milk Surveys

During the last three years, 1954, 1955 and 1956, three surveys have been made of fluid market milk to determine its content of antibiotics. In the first survey, a variety of dairy products was tested, including fluid milk, powdered milk, evaporated milk, ice cream, butter and cheese, as well as shell eggs and broken eggs. Ninety-four quarts of fluid milk were tested for antibiotic activity. Three quarts, or 3.2 per cent, were found positive for penicillin. No other proven antibiotics were found in any of the other products. In the second survey, 474 samples of market milk were tested and 11.6 per cent contained penicillin. The concentration varied from 0.003 unit/ml. to 0.08 unit/ml. (highest amount, 80 units/liter). In the third survey, 1,706 samples were examined; these were collected from all 48 states and the District of Columbia. This extensive survey showed penicillin present in 5.9 per cent of the samples examined. The concentrations ranged from 0.003 to 0.550 unit/ml. (highest amount, 550 units/liter). In addition, one of the penicillin-positive samples showed streptomycin activity and 17 samples (approximately 1 per cent) appeared to contain bacitracin, one of the tetracyclines, or a combination of these drugs. In every case the presence of penicillin was confirmed by the penicillinase identity test, while the other antibiotics could not be specifically identified.

Significance of Increase in Positive Samples

The marked increase in the number of positive samples in the year separating the first and second surveys caused some concern, and it seemed advisable to obtain some opinion on the possible public-health significance of these quantities of penicillin in market milk. Accordingly, some 30 authorities in the fields of antibiotic therapy, allergy and pediatrics were asked to express an opinion concerning their views as to the possible public-health significance of these quantities of penicillin in market milk. The majority of these experts believed that these amounts were unlikely to modify the oral or intestinal flora, cause the emergence of resistant strains, or provoke sensitization of an insensitive person. However, the majority felt that such concentrations might possibly cause a reaction in a highly sensitive individual.

It is estimated that about 10 per cent of our population have a "proneness" to become sensitive during their lifetime to some food,

drug, or other substance, while the great majority of individuals are resistant. Within this 10 per cent there is a great variation in susceptibility to sensitization. Some acquire it readily, while others show various degrees of resistance. The allergic manifestations also vary in degree from mild transient rashes to prolonged urticaria and from a brief asthmatic attack to fatal anaphylactic shock. It is this latter reaction with which we are most deeply concerned. All of the antibiotics used in mastitis preparations except penicillin have a low sensitization potential and none except penicillin has been so widely associated with fatal allergic reactions. Thus, our major concern is with penicillin.

To cope with the problem, the Food and Drug Administration extended an invitation to a group of physicians to form a medical advisory panel to consider the public-health problems involved in the presence of antibiotics in market milk. Following an all-day session, during which the problems involved were discussed thoroughly, it was apparent that our main health problem is concerned with penicillin to the exclusion of the other antibiotics that are used in mastitis preparations. It was the consensus of the panel that antibiotics such as the tetracyclines, bacitracin, polymyxin and neomycin—all of which may be found in mastitis preparations—do not pose a public-health problem as used in treating mastitis. It was agreed that penicillin is a highly antigenic substance and, even in the small concentrations found in milk, might well cause reactions in highly sensitive individuals.

Steps Taken Recently by FDA

During the past few months, the Food and Drug Administration has taken three steps to alleviate the public-health problem involved:

(1) Through cooperation with the United States Department of Agriculture, an intensive program has been initiated to educate the farmer concerning the importance of not using milk for human consumption from cows treated for mastitis with antibiotic drugs for a period of three days following the last treatment. The National Milk Producers Federation, which reaches some 500,000 farmers, is assisting in this education program through their state agents.

(2) On January 23, 1957, we published in the *Federal Register* notice of a proposal concerning the warning statement to be required on antibiotic drugs intended for intramammary infusion. This warn-

ing was to be placed on the immediate container of the drug rather than in the literature accompanying it.

(3) On February 9, 1957, a notice of proposed rule-making was published in the *Federal Register,* limiting the penicillin content of mastitis preparations to 100,000 units per dose.

It is hoped that these steps will alleviate the problem of antibiotics, particularly penicillin, in our milk supply. However, if these procedures are unsuccessful, it may be necessary to ban the use of penicillin in mastitis preparations in the United States.

The control of antibiotics in our food supply becomes more complex daily. We have before us now for consideration the use of chlortetracycline and oxytetracycline in fish as a means of extending "shelf life." Unfortunately, in contrast to poultry, we have been unable to demonstrate that ordinary methods of cooking (broiling, frying, boiling or baking) treated fish eliminate the residual antibiotic. Furthermore, some fish are eaten raw; in both cases the consumer would ingest antibiotic residues. Before tolerances can be established for these antibiotics in fish, it will be necessary for those requesting tolerances to demonstrate that the residues found are not dangerous to the public health.

Looking to the Future

As we attempt to feed more and more people better and better and as more and more uses are found for antibiotics in foods, those charged with the responsibility of seeing to it that such foods are safe will find their positions increasingly difficult. In the United States we plan to move slowly and cautiously with each new proposal concerning antibiotics in foods, keeping in mind that if the public or any unfortunate segment of it has reservations concerning the safety of our food, it must at the same time question the effectiveness of our operations. **[The End]**

• LONDON DINNER HONORS FLI •

On the evening of July 26, a dinner was given by the Food Group of the Society of Chemical Industry, the Society for Analytical Chemistry and the Association of Public Analysts, honoring The Food Law Institute. The testimonial party was held at the Hall of the Worshipful Society of Apothecaries of London.

Following the dinner, toasts were proposed to Her Majesty, the Queen; to The Food Law Institute; and to the assembled guests. The FLI toast was proposed by Sir Harry Jephcott.

THE CONTROL OF

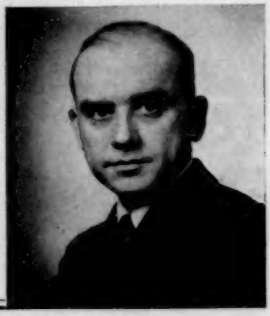
Chemical Additives (Other than Antibiotics) in Foods

By C. A. MORRELL

Dr. Morrell, in This London Meeting Paper, Notes That Governments Should Take Whatever Feasible Measures Are Needed to Protect Public Health and Maintain Consumer Confidence

WHEN I WAS ASKED to present a paper at this meeting today, I wondered why this subject was chosen as the theme of an international symposium. There are many other topics from which the speakers might have selected interesting items for discussion. However, after consideration, I concluded that the program committee had chosen wisely because the question of just what to do about the use of chemical additives in foods is one that is being considered in many countries. How serious is the matter and what legislation or restrictions are essential to the public interest? No one should want to impose restrictions arbitrarily on business. We need sound reasons before we can demand that manufacturers spend considerable money in collecting and supplying information about new products or procedures and we want to lay down a pattern or "drill" that provides just what is necessary and no more. I know that whatever is spent on obtaining data and information must be collected from the public through the increased price of the foods in question. We have to know how much is enough and what pattern to impose. These questions are not yet answered in the minds of all of those concerned with the matter.

The matter, too, is one of international importance, since there is a great deal of international trade in foods, both processed and raw.



The Writer, of Ottawa, Canada, Heads the Canadian Food and Drug Directorate There

It would be a great help to importers and exporters of foods if the methods of control of the use of chemical additives in various countries were identical or at least very similar. It seems, at the moment, that there is not the same degree of interest in all countries, at least at the official level. One wonders if some of us are overly exercised and if others are not sufficiently aware of the potential dangers of this trend in the food industry.

Furthermore, the safety of the substances under the conditions of use to which they will be put can be determined only after a great deal of work in many fields of science. I am sure it is a task that we in Canada cannot do alone and I doubt if any one country can deal thoroughly with the many products already proposed for use in or on foods in a period of time that is reasonable and practical from the commercial viewpoint. We need help from the facilities of all. What, then, is the present situation? What can be done to improve it?

It has been recognized by the governments of a number of countries and by international organizations that the increasing use of chemical substances for one purpose or another in or on foods presents a considerable problem to those responsible for protection of public health. Although some governments have taken official notice of the addition of chemicals for a great many years, through the promulgation of regulations and other laws controlling the maximum amounts that may be present, the problem was not so acute or extensive in the past.

Furthermore, it is only recently that the public has been conscious of changes in methods of food production, processing and marketing which involve a greater use of an increasing number of chemical substances. They are conscious that something is happening

without actually knowing what is going on. Those connected with the food industry—either in production or control—are, of course, aware of the expansion in this field that has taken place since the war. The press and consumers have displayed some evidences of uneasiness, if not alarm, about the safety of their food supply under these circumstances. In Canada, letters from women's organizations, articles in the press and questions in the House of Commons have requested some assurance that the government does provide the necessary protection against possible health hazards from this source.

I suggest that government has two functions in this situation. One is to take whatever feasible measures are available and necessary to protect public health; the other is to maintain the consumer's confidence that his food is safe and wholesome. At this point we may well ask if there are serious hazards presented by these chemical substances in our food supply. This is a question that can be answered "yes and no." The answer is "yes" if they are present in large quantities and "no" if the amounts are sufficiently small. Rational methods of dealing with chemical additives will, then, involve the setting of tolerances. By "tolerances" I mean the maximum amounts of possibly harmful substances that will lawfully be permitted in or on foods intended for human consumption.

The situation is not entirely new. We have had considerable experience in the past. The use of coal-tar colors is not new; preservatives have been used in foods for many years; bleaches and other chemicals have long been employed in basic foods; and arsenic has been an ingredient in insecticide sprays for a long time.

In my own country in the bad old days of more than half a century ago, it was possible to point to a number of treatments to which food was subjected that were not only outright frauds, but which were also unquestionably dangerous. It is difficult to discover recent outbreaks of illness that can be positively attributed to chemical additives. I am speaking, of course, of acute illnesses—ones that occur immediately after consumption of foods or shortly thereafter and that can be traced to a chemical additive. Such outbreaks have been rare or nonexistent in Canada in the last 40 years or, at least, there is no record of them. In other countries I believe there have been some occurrences of this kind.

On the other hand, one must consider what can possibly result from the long-continued consumption of small amounts of chemicals—

amounts that are not capable of showing any immediate and easily discernible effects but which nevertheless develop effects so gradually that they are not connected in our minds with the cause. The amount and kinds of disease so produced are certainly in the realm of speculation at the present time. If positive and convincing evidence in that direction were available, there would indeed be no arguments against governments' taking the severest restrictive action to control the addition of chemicals to foods and to prohibit chemicals where necessary.

In spite of the lack of direct evidence from our experience that outbreaks of acute chemical poisoning from foods have occurred in Canada and despite the fact that we have no evidence that a mass chronic poisoning is developing among Canadians from the use of chemical additives, the Canadian Government is employing whatever measures are available to it through the Food and Drugs Act to assure that such an undesirable situation does not occur. This is, I believe, a proper exercise of its authority in the public interest.

I would suppose that all citizens support the government in this activity. They all wish to benefit by the best and latest commercial practices in producing, preserving, processing and presenting in the most attractive manner a great variety of foods at as low a price as possible, but they have a suspicion that they are unable to judge for themselves what may safely be done and they prefer to have a competent technical group, over which they have some control, exercise authority objectively in their interests. I do not mean to imply that a particular government department contains the only group of people qualified to speak intelligently on the citizens' behalf. Indeed, the chemical and other industries concerned have well-trained, intelligent and responsible employees who are often well aware of the properties of the substances they use or propose to use; furthermore—and, perhaps, what is more important—they are also aware of the gaps in their knowledge of these chemicals. The public preference that the government exercise its authority to establish a reasonable control to assure safety of the food supply is based on the fact that the government represents them and their interests. No complex game that is played with such competitive vigor by so many people of all types as is the marketing of foods can be played properly without a code of rules and without a strict and impartial referee to enforce the code on one and all alike. I argue that there is a need for a code and a referee in this field not only to protect the public from the possible results of

competition, but also to protect the players from one another. The government is the proper agency to assume the role of referee.

But the body of referees must have a clear and practical code to enforce or their efforts will only add to the confusion. This pattern or code is still a matter for argument in many countries and is also a subject for international discussions such as this one.

The argument may be raised—perhaps with some cause—that such action by a government, if thoroughly and diligently carried out, is an obstacle to progress in the agricultural and food-processing and -marketing fields. It is feared that it will hamper the employment of new chemicals in desirable processes because of delays in clearance of information by the civil service and that civil servants will be capricious or unnecessarily demanding in respect to the evidence required to convince them as to the safety of a product. Considerable experience in clearing new-drug submissions in Canada does not show that this argument has any substance. In any truly democratic system of government there are adequate means available to the industries subject to control to prevent any capricious or stupid interference with real progress. This fear does point up, however, the need for some clear and understandable code of rules under which the referee and industry must operate.

If one agrees to the premise, which seems to me incontrovertible, that governments must accept—within the limits of what is possible—the responsibility for assuring the safety of the public food supply, it becomes a question of how this can be done. The decision as to how much of a chemical may, with safety, be added to a food is one that should be made by a department of government primarily concerned with the health and welfare of the public. This is a control function and not one that should be involved with production. The better industries have recognized in their organizations that control departments must not be responsible to those whose main business is production. Too often a conflict arises, leading to pressures that may cloud the judgment of those who must decide whether a particular product is safe. It is better, therefore, to separate the two functions. This does not preclude the necessity for those required to make the decision to take into account the advantages of admitting another chemical substance into our foods. In some cases it will be a matter of weighing a calculated risk, but except in a dire crisis the risk must be trivial if it is to be accepted.

Why Industry Should Supply Data to Referees

Before making a decision as to how much of a chemical may be added to a food, the referee body must have before it adequate information on which to base the decision. It seems to me reasonable to expect that the necessary information and data will be supplied by the industry advocating the use of the substance in question. Not only will that industry derive a financial benefit from the sale of its product, but very often knowledge of the properties of the substance is at first possessed only by its employees.

Furthermore, one must consider that the government department or bureau will always have very limited facilities and numbers of personnel in comparison with its responsibilities in this field and others. I believe it would not be acceptable to taxpayers for the government to engage in research on a virtually unlimited scale to satisfy the demands of specific groups of citizens for information that in many cases would not benefit the country as a whole and, in cases of failures to develop something useful, would benefit no one except those employed to carry out the investigation.

This is not to say that some types of investigative work on chemical additives in foods should not be carried out by government departments or agencies, but that the work of the government control authority will have a different emphasis or, possibly, a different direction from that required by industry. Research of the type concerned with specific information, either in confirmation or refutation of claims, or for the purpose of developing quantitative methods of analysis or the establishment of standards is often necessary.

The information demanded for review before there can be any agreement that a particular product may be safely used in or upon a food must necessarily be convincing and as complete as is required for the purpose. This, perhaps, is the most contentious point in the problem as a whole. I believe that most manufacturers and processors, as well as producers, of foods are quite prepared to accept a government department or agency as the arbiter in deciding what tolerance for a new chemical in foods is a safe one, provided that they can also agree as to the amount and kind of information they must supply to satisfy the judicial body. If no distinct pattern of experimental data can be outlined for the purpose, the decision might be indefinitely delayed by requests for other types of information or further elucidation of particular points.

The question then arises as to how much is enough. This is the crux of the subject before us. There are those who say that every new chemical proposed for use in foods presents an individual problem and that no detailed plan of examination can be followed. While I agree that there will be individual differences in the detail of studies depending on the nature of the substance in question and what use is to be made of it, I believe that some general pattern of tests can be laid down and, indeed, is necessary. As a matter of fact, patterns have already been established and are being followed in some countries. The trouble is, of course, that equally qualified experts elsewhere do not agree that they are in all aspects the right ones. When experts disagree, what can the administrator do? I believe he must accept the advice of his own experts or get the experts together to settle their differences. This is a place in which international organizations such as the World Health Organization and the Food and Agriculture Organization can play an extremely useful part. It is encouraging to know that both WHO and FAO have displayed active interest in this field; I suggest that their efforts should be strongly supported by those administering legislation applicable to this field of public health.

Clinical Tests and Relationships Between Tolerances

While I cannot anticipate all the tests a new chemical should undergo before it is used in our food supply, there are two points that might well be mentioned:

The majority of the investigations of a biological nature are necessarily carried out on animals and the results must be interpreted in terms of human safety. This is believed to be an uncertain procedure and it is a contentious one. In our investigation of new drugs we properly require evidence of safety both from the laboratory and the clinic. What part should the clinical trial play in the gathering of evidence for the safety of chemical additives? The problem of the new chemical additive is different from that of the new drug in that it is not intended to be used in an amount that will produce any effect on the consumer of the food. In fact, our purpose is to make certain that the amount used has no influence whatever on his physiology or structure. Can this amount be determined with certainty when tests on animals are the only ones used? I hope that the answer for practical purposes will be "yes" because of the amount of work and time and money that would be necessary otherwise.

The other point that deserves a clear statement is the relationship between the tolerances set for each chemical substance and the largest amount that may be used with certain safety. In my opinion, these need not be the same. I believe the principle to be followed is to set the tolerance no higher than is necessary for the purpose for which it is used. In most instances this would be much lower than the amount that could be safely used. There is no harm in this, and it is wise to discourage the use of unnecessarily large amounts of chemicals in our foods. Again, may I point out how convenient it would be for international trade if the same tolerances were adopted by all countries for each permitted chemical additive.

Finally, I believe that tolerances should be established for all new chemicals, needed in our food, but which present possible hazards. These include colors, pesticide residues, preservatives, emulsifiers, etc. However, no tolerance should be established until satisfactory evidence is available upon which competent authority can predict that no harm will result from the specified use of the substance in question under the conditions permitted. Until that time such substances should not be used in food.

Once again I say that the subject of chemical additives is one of great international significance and that we need a clearing house for information and guidance in obtaining some measure of uniformity in dealing with the great number of chemical substances now being put forward as of some value or other in producing, processing or preserving our food. Actually, I would like to have assurance that some of the chemical additives proposed do have some value that makes their use necessary. I often wonder if the industry is not moving too fast and going too far. However, I do not wish to stand in the way of progress!

Although it is not often discussed, there is another aspect of the chemical-additive program that deserves some consideration. I do not believe that any chemical additive should be used if the main or only result of its use is deception of the public as to the true value or nature of the food. This comment might well apply to the improper use of colors or, indeed, of any chemical if it contributes nothing of advantage to the consumer. Those who are considering legislation in respect to chemical additives might well bear this in mind. Protection of the public from both health hazards and fraud is the paramount purpose of such legislation. **[The End]**

Antibiotics in Foods

By C. A. MORRELL and F. S. THATCHER

This Analysis of Acceptable Drugs and of Measures to Prevent Degradation of Their Medicinal Worth, With Assured Safety of Resulting Foods, Was Prepared for the Joint Meeting by Dr. Morrell (See Foregoing Article) and Dr. Thatcher, Microbiology Head, Canadian Food and Drug Directorate

FEW technical developments in food-processing have aroused more widespread interest and controversy than the proposal to use antibiotics as preservatives in foods.

The addition of so many chemical additives to foods has raised a serious question as to the safety of the products used. These products, however, do not usually have other important uses which cause them to be ingested or otherwise come in contact with the body. Antibiotics are different. Their main use has been and still is, in the cure or treatment of serious diseases. Their continued value in treating these diseases is of outstanding importance to individuals and to public health in general. It would be quite unwise to permit other—really nonessential—uses of antibiotics, if in doing so their value and use as therapeutic agents was either lessened or made dangerous. The employment of antibiotics in foods requires limitations and other measures to prevent the degradation of their medicinal worth, and also assurance that the resulting food products are safe in themselves.

While present commercial interest has been largely limited to the use of a closely related group of antibiotics—the tetracyclines—and primarily for the control of bacterial spoilage in fish and poultry, it may be anticipated that the trend will continue and lead to proposals for the use of other antibiotics over a much broader range of applica-

tion. Several appealing claims have been made in relation to the practice: delay of the onset of bacterial spoilage and consequent prolongation of the "shelf life" of perishable foods; the expansion in marketing ranges; the food-conservation of potentiality in a hungry world; the contribution to an improved diet that might be made in technologically undeveloped countries; its introduction with a minimum capital requirement. All of these must be weighed in perspective with the complex public-health aspects germane to a widespread distribution in foods of chemicals with potent but only partly understood biological activities, the importance of which in medical treatment has been so amply demonstrated.

The purpose of this presentation is to discuss these practical and public-health issues as they are related to the Food and Drugs Act of Canada.

In order to satisfy the requirements of the Food and Drugs Act, a proposed introduction of new chemicals into foods requires that two basic questions be posed; the law requires that decisions be made in accord with the answers to these questions. The questions are: Does the introduction of such chemicals create a hazard to health? Does their introduction into foods offered for sale perpetrate a fraud? To negate this latter inquiry would require that the proposed substances fulfill the claims made for them and that their use represents an advantage to the consumer over currently accepted practices directed to the same end.

Any action that might be taken involves important considerations, such as existing regulations, the administrative policy of the responsible directorate, and enforcement problems—all viewed in the light of the intent of the Food and Drugs Act, which is to function in the interest of the consumer. Thus, when the first submission was received to allow the use of specific antibiotics as food preservatives, the act and existing regulations contained no provision to allow the inclusion of such substances in foods. Would consumer interest be served by recommending to the Minister that the regulations be amended? In the light of past experience, which teaches forcibly the need to take every precaution for the safeguarding of the future in relation to consumer health and fraud: What experimental evidence was available to justify a recommendation to amend the regulations? What was the experience from use of the proposed antibiotics in allied usage (as for instance in animal feed) and in therapy? What

were the "gaps" for which new experiments would need to be undertaken? Were adequately sensitive and practicable methods of assay available? What enforcement problems could be foreseen to prevent abuses? What mechanisms, staff and training would be necessary for enforcement of any new regulation; would "labeling appeal" be misleading to the consumer in that the "psychology" of "wonder drugs" might persuade the consumer to purchase even though the product might have been exposed for sale for a period longer than the duration of any protective effect of the antibiotic? What was the potentiality for fraud by treating and affixing a label to a product already contaminated beyond the power of the antibiotic to restrict bacterial growth?

In addition to these problems of administrative flavor, a scientific appraisal would need to be made of the whole question of any potential health hazard that might arise through toxicity (acute, chronic or accumulative) of the antibiotics or of their decomposition products or those derived from reaction with food ingredients, their carcinogenicity, propensity to induce allergy, the development of antibiotic-resistant pathogens or spoilage microorganisms, the effect of a disturbed microbial ecology on quality and spoilage, modification of food-poisoning probabilities and any "rationale" for expecting the mode of action of antibiotics in microbial cells to have parallel implication in human cells. It was essential that justification for use of antibiotics in foods for human use should meet the challenge of an examination of this nature.

Condensed below is the outcome of such an enquiry undertaken with particular reference to the tetracyclines. It is beyond the scope of this report to attempt to summarize all of the vast literature on the topic.

Practical Limitations

The effectivity of antibiotics as food preservatives is subject to many variables which impose practical limitations to their probable usefulness. Outstanding among these variables are: (a) the nature of the food, (b) the initial degree of contamination of the food at the time of antibiotic treatment, (c) the generic type of dominant contamination, (d) the adequacy of sanitary and hygienic practices observed during processing and marketing of the foods and (e) the antibacterial range of the antibiotic used. To illustrate briefly:

Different species of fish respond differently to the preservative action of chlortetracycline (11) * while it has been reported (3)—though with recent indication of contradiction (1)—that the use of this antibiotic in shucked oysters is not warranted. Neither is there general agreement on its usefulness in shrimp or crab meat (22). It has been suggested that the comparatively high pH values of these latter foods promote more rapid inactivation of the antibiotic. Experience has shown that foods which are heavily contaminated directly and immediately or which have been held under conditions that have allowed bacterial multiplication do not respond favorably to the use of the tetracyclines, while if the dominant contamination should consist of yeasts or fungi or of specifically resistant strains of bacteria, the antibiotic again will be without effect.

Thus, the use of antibiotics in foods which have been handled, processed or stored under conditions not in keeping with satisfactory standards of sanitation and hygiene cannot be expected to have a significantly longer shelf life. Further, the antibiotic cannot allay the process of spoilage once it can be detected. These observations have given rise to two attitudes: (a) The use of antibiotics to prolong the shelf life of perishable food tends to be more effective in accord with advancing standards of factory sanitation; hence, an incentive to this latter end is introduced to the food trades by use of antibiotics. (b) Food that is to be frozen and is produced under high standards of sanitation (which includes the technological factors of time and temperature) has no need for the use of an antibiotic. This latter subject is still one of considerable controversy among fisheries experts. In addition, it should be emphasized that if the "extra" days of shelf life are to be used in transit to market areas further afield, the hazard of exposing for sale food of very low quality is to be contemplated unless rigid hygienic marketing practices are adopted.

Effects of Antibiotics in Food

It is now clearly established that chlortetracycline and oxytetracycline, when used in specific foods in accord with the recommendations from the promoting companies, can exert a bacteriostatic effect against representatives of many bacterial genera; in consequence, the onset of bacteriological spoilage is delayed for a variable number of days depending on conditions of storage and the initial degree of

* All parenthetic numbered references are to list at end of article.

contamination (4, 6). In the treatment of fish or poultry, the usual procedure has been to pack the product in ice into which the antibiotic has previously been incorporated or to immerse the product in a solution of the antibiotic at some critical period in the processing scheme (4, 6, 22).

The same and other antibiotics have also been used experimentally for other types of foods and by other methods. For "red meats," these methods have included the feeding or intra-arterial or intraperitoneal injection of antibiotics prior to slaughter (9), the killing of whales by the use of missiles containing an explosive "head," which frees substantial quantities of an antibiotic into the wound and which is carried through the muscular tissues during the animal's "agonal" period or by the addition of antibiotics while inflating the peritoneum of a killed animal (22). Specific antibiotics that have proved of little value in the preservation of animal foods may reduce the incidence of particular types of spoilage of leafy vegetables or fruits (9).

Mode of Action of Antibiotics

The basis of selection of antibiotics for food preservation and also an evaluation of some aspects of potential health hazard is aided by consideration of the mode of action of antibiotics.

In general, antibiotics may be either bacteriostatic or bactericidal. In the former instance, even if only susceptible strains of bacteria are present in a given food, addition of a bacteriostatic substance can merely inhibit multiplication for such time as the concentration of the agent is beyond the threshold level. If such an antibiotic is rapidly inactivated in foods, the duration of its preservative action will be brief. Further, if substantial microbial growth has occurred prior to bacteriostasis, extracellular enzymes conducive to spoilage are still free to function. Chemicals that are bactericidal tend to be less specific in action and may have a greater tendency to be toxic to nonmicrobial cells. Antibiotic substances vary widely in the "range" of species and genera that are subject to them. No antibiotic has yet been found that destroys all genera of microorganisms, and such a substance with the factors of safety necessary for use in foods is not a foreseeable likelihood. The range of activity against representatives of different taxonomic groups is a highly specific property.

The tetracyclines have been the subjects of initial choice for commercial food preservation because they are able to inhibit the

growth of bacteria among widely different taxonomic groups, including Gram-positive and Gram-negative bacteria though not all members of either group. Penicillin, on the other hand, tends to have a more limited spectrum and is mainly active against Gram-positive bacteria; it is therefore not satisfactory for food preservation because a great many food-spoilage organisms are Gram-negative. Streptomycin is similarly limited, though effective against several Gram-negative species, while polymyxin seems to be restricted in action against a small group of Gram-negative bacteria. Thus, if used singly, none other than a "broad spectrum" antibiotic could be expected to offer effective preservation because of the inevitably diverse nature of contaminants that have access to foods. None of the antibiotics named above have significant action in foods against yeasts or fungi (23). If initial contamination or other factors are conducive to growth of yeasts or fungi, the presently used antibiotics will not only be of no avail, but the possibility must be entertained that by removal of potentially competitive bacteria the residual microorganisms may indeed grow more readily.

The precise mechanisms involved in the antibacterial effects of antibiotics is not fully understood. Umbreit concludes that the function of each antibiotic is dependent upon its molecular structure as a whole and not merely upon the presence or orientation of individual structural groups (25). This may offer teleological explanation of the marked specificity of different antibiotics.

The tetracyclines currently of dominant interest in foods have been reported to inhibit several enzyme systems. Much interest has been directed towards their "uncoupling" effect in oxidative phosphorylation as a basis of their bacteriostatic action, though Umbreit (25) does not accept this as an adequate explanation. Other mechanisms inhibited include respiration, fatty-acid oxidation, arginine catabolism, nitro-reduction, and adaptive enzyme formation (29). The tetracyclines are known to be active chelating agents, and hypotheses have been advanced to infer that antibacterial action may result from the removal of essential cations from the environment of enzymes requiring metallic prosthetic groups or that enzymes may be inactivated by reaction between the antibiotics and essential cations already attached to enzyme molecules (29, 20).

The specificity of antibiotics in mode of action may be illustrated by comparison of the tetracyclines with penicillin and streptomycin.

Penicillin inhibits an early stage of ribose-nucleate synthesis (25). The functional site of streptomycin has been suggested to be the inhibition of an intermediary reaction between pyruvate and oxalacetate, which Umbreit postulates to be the formation of 2-phospho-4-hydroxy-4 carboxyadipic acid. Such specificity of function points to the requirement that the assessment of the desirability of an antibiotic in foods should be based on the specificity of each antibiotic. Acceptance or rejection of each individual compound must be independently based on its total specific properties, including, of course, those which affect the degree and kind of hazards to the health of the consumer.

Arising from specificity of function is the further consideration germane to our appraisal of the safety of antibiotics in foods—namely, since many of the reactions inhibited in bacteria are known to occur in mammalian cells, to what degree could similar inhibitions be activated in mammalian cells if subjected to prolonged exposures to antibiotics present as ingredients of a daily diet? No adequate answer to this latter problem is forthcoming other than an indirect deduction from toxicity data, though evidence has been presented to show that a selective permeability difference between susceptible bacterial cells and mammalian cells, or particulate cell fractions within them that contain the susceptible enzymes, may explain mammalian-cell resistance to streptomycin (26).

Microbial Resistance to Antibiotics

In addition to the significance of the comparative resistance to antibiotics of microbial and mammalian cells, the evaluation of antibiotics in foods is rendered more obtuse by the various resistance phenomena demonstrated by microorganisms. Intergenus and interspecies differences in susceptibility and resistance to a particular antibiotic have been mentioned already. Differences also are recognized among different strains within a species. Hence, all antibiotics exert some degree of selectivity so that from any mixed population of microorganisms a residuum of survivors is to be expected. This picture is further complicated by the well-established phenomenon of the development of resistant populations induced by exposure to an antibiotic and is recognized as an important limiting factor in the therapeutic value of antibiotics, particularly with respect to the staphylococci (8, 12). The risk of inducing antibiotic-resistant pathogens by exposure to antibiotics in food and the consequent impairment of the therapeutic value of antibiotics was a commonly

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voiced fear during the exploratory stages of the use of antibiotics as food preservatives. Recent statements suggest that these fears, while rationally founded, may have little support in experience. A statement by Eagle (10) has been quoted frequently: "There is no evidence whatever that small concentrations of antibiotics which do not kill bacteria have any effect on the resistance of the strain."

Induced resistance is widely recognized as a mutative change in the gene structure of a previously susceptible cell (5, 25, 31). The antibiotic is said not to cause the mutation, but allows selection and survival of the progeny of the mutant cell (15). Resistance may also occur through a physiological adaptation dependent upon the synthesis of adaptive enzymes which permit an alternative pathway for some essential function normally inhibited by the antibiotic (29). Induced resistance to one antibiotic may confer resistance to certain others (17).

An important observation in the public-health appraisal of these mechanisms in relation to foods is the demonstration that different antibiotics have different propensities for inducing resistance and, further, that the occurrence of specific resistance becomes manifest in two ways. A "step-wise" development of resistance may occur wherein the majority of surviving resistant cells and their progeny have a tolerance to the activating antibiotic only slightly greater than the concentration to which they have been exposed. An increase in concentration will further inactivate a proportion of this population so that resistance to a high level of an antibiotic would require multiple exposures to progressive concentrations (12, 31). The tetracyclines at low concentrations generally behave in this manner and on this characteristic the argument may be based that the single exposure to the low level recommended for use in foods is not likely to induce resistance to the much higher concentrations therapeutically used. Certain other antibiotics such as streptomycin are more prone to induce resistance to an extremely high level which may exceed that established in the blood during therapy as a result of one or few exposures (16). A wide difference in comparative hazard between the two groups will be recognized. The development of microorganisms resistant to antibiotics, apart from any potential threat to their therapeutic value, further complicates the potential problem of selective survival already touched upon.

The observation has been made frequently that whenever the normal microecology of a mixed population is disturbed by any

selective process, the risk arises that specific populations or species normally held in check by competitive microbial action may become dominant and, on occasion, may give rise to new forms of spoilage not normally encountered. This has been shown during the use of sorbic acid to control yeasts in pickle fermentations or in the suppression of molds in cheese. In the one instance, gas-forming lactobacilli have caused unusual spoilage; in the latter case, sorbic acid has allowed the proliferation of clostridia with objectionable spoilage propensities. Comparable effects may arise where antibiotics are the equilibrium-disturbing factor, a condition already encountered where nisin has been used in cheese. The occurrence of dominantly resistant populations could soon invalidate the use of the antibiotics to which resistance has been induced. An argument against such probability is provided by the assumption that each incoming consignment of untreated food will have had no previous contact with an antibiotic so that each production-unit of food, while it may contain naturally resistant species, will not receive repetitive exposure. This presents further reason to avoid antibiotics which commonly induce "one step" high-level resistance. The argument may prove invalid if contamination of foods occurs through resistant organisms that may have become endemic in ships, conduits, machinery, factories or workers' clothing as a result of repeated exposure. The need for exacting cleansing and sanitary processes is again indicated. Experience alone can determine the outcome of such potential hazards.

Pathogens in Food

The effect of antibiotics added to foods containing pathogens has been considered from the point of view of increasing the incidence of resistant strains of pathogens and the propensity for toxigenic species to cause food-poisoning. Use of low levels of an antibiotic having the "step-wise" tendency to induce resistance is considered unlikely to contribute significantly to the former problem for the reasons already discussed, though if a resistant pathogen is already present in the food, the risk of increase in numbers due to the selective effect of antibiotics must be considered. The occurrence of this phenomenon is discussed by Finland (12).

Widespread experience in the use of the tetracyclines in poultry and animal feeds does not seem to have given rise to undue problems from resistant pathogens, an opinion also expressed by Finland (12) and by Hines (13) in a recent review of the topic. The few exceptions

that have come to our attention have been associated with abuses in the quantities of antibiotics used or through lay treatment of disease in poultry flocks.

From limited studies, it has been concluded that chlortetracycline in fish reduces the numbers of added staphylococci and *Clostridium botulinum*, so that no evidence for selectively favored survival of these organisms exists (22). Evidence is still needed, however, to establish the effect of antibiotic treatment of foods containing *antibiotic-resistant* staphylococci, though it is proper to relate any such data to the fact that antibiotic-treated food, to secure any potential advantage from antibiotics, must be processed and stored under favorable conditions of sanitation, which implies that an environment conducive to toxin formation will not be permitted. The discovery of strains of *C. botulinum* resistant to nisin and subtilin, the antibiotics that have received experimental use as adjuncts to canning, is a powerful argument against such use of these antibiotics in canned foods, but experiment continues with canned acid foods not subject to botulism (2).

Toxicity of Antibiotics and Residues

It would seem axiomatic that no chemical should be added to foods for general use unless it can be shown to be nontoxic at the levels and under the conditions of use likely or recommended. Accordingly, this aspect of the present problem has received careful examination in relation to the use of the two antibiotics (tetracyclines) for which submissions have been received.

An extensive review by Hines (13) has been published recently of the literature on the toxicity of chlortetracycline when administered over prolonged periods to laboratory animals, poultry, swine and man—the last including premature infants, infants and children, adults and geriatric patients, all in comparatively large numbers. The reviewer concluded that "there is no evidence to indicate that the prolonged oral administration of chlortetracycline to man or domestic animals is harmful at presently recommended dose levels." These levels refer to ingestion in feeds or to therapeutic usage in amounts which greatly exceed those presently recommended for use as food preservatives.

In the light of the differing specificity of action of antibiotics and their differing potential health hazards, each different antibiotic must be assessed independently, though oxytetracycline, chemically very

similar to chlortetracycline and of comparable effectivity, has also shown similar lack of toxicity.

The nature of the inactive decomposition products of the tetracyclines is poorly understood. Several products of hydrolysis have been described during determination of the chemical structure of these compounds (14, 27, 28), but the extent to which these occur in foods during inactivation is not known. Some of these are naphthol derivatives. Barnes (2) refers to a product named "isoaureomycin," which seems to be a normal degradation product of chlortetracycline in animals: "Rats have been successfully maintained on a diet containing 1% isoaureomycin for 6 months."

Carcinogenicity

Direct studies to investigate the carcinogenicity of antibiotics are unknown to the authors. The deduction has been made that if carcinogenesis were a property of these compounds, this fact would probably have been revealed during the vast clinical experience associated with antibiotic chemotherapy.

Nevertheless, careful observation seems indicated in the light of a study which shows that mice receiving antibiotic treatment during experimental transplantation of lymphosarcoma cells showed a higher incidence of successful transplants when using sparse inocula and that tumors in resistant mice showed greater growth before demonstrating the normal tumor recession (19). Oxytetracycline and chlortetracycline did not exhibit these properties.

Allergic Sensitivity

Certain antibiotics, such as penicillin, have been shown to induce various allergic responses ranging from comparatively mild urticaria to severe anaphylaxis. Such enquiry as has been possible would indicate that allergic reactions in response to the tetracyclines are rare if they occur at all. No bona-fide case has come to our attention and we are assured that no such occurrence has been established among production workers or those who are in constant contact with the tetracyclines used in animal feed. Rein (18) states with regard to the tetracyclines: "Hypersensitivity to these antibiotics, even when applied topically, occurs infrequently."

Effect of Antibiotics on Intestinal Flora

A great deal of literature has been published on this aspect, mainly directed towards clarifying the basis for stimulated growth rates established among poultry and cattle and, with less evidence, among human babies. Several reviews are cited by Finland (12), by Sieberth and others (21) and by Combs (7). Modifications do occur, with the general inference that they are beneficial in the instance of the tetracyclines (13). The evidence for lack of toxicity by the oral route would suggest that the change in intestinal flora does not exert adverse physiological effects (13), but this needs to be considered in the light of the common clinical finding that continued use of an antibiotic may allow the selective multiplication of antibiotic-resistant flora, with subsequent development of disease such as staphylococcal gastroenteritis (8) and various manifestations of noniliasis (12). The death from enterocolitis of chinchillas fed chlortetracycline-enriched feed has been reported recently. Resistant staphylococci were isolated from the animals (30). These occurrences offer a strong argument in favor of the restriction of the levels of antibiotics tolerable in foods to those levels which disappear completely during normal cooking of the specific foods. Data on hand show that the concentrations of the tetracyclines currently recommended for use in fish or poultry are effectively destroyed during normal cooking, and are in general accord with those of Tarr (22) and Tomiyama (24).

Synergistic Effects of Antibiotics

Synergism between specific antibiotics is well established. It is to be expected that synergistic combinations will, in the future, be proposed for use in foods.

The effect of such combinations will need investigation in the light of the modified functions of a synergistic combination as distinct from the component entities.

Conclusions

The conclusions deduced from the foregoing discussion and offered as indicative of the opinion of the Food and Drug Directorate are as follows:

The only antibiotics acceptable for use in the light of present knowledge are those with the following properties: They (a) possess

a "broad spectrum" antibacterial action, (b) are nontoxic within acceptable limits of safety, (c) demonstrate no common propensity to induce "one step" high level resistance among a microbial population, (d) are noncarcinogenic, (e) are nonallergenic, (f) are stable under conditions of use for a sufficient period of time to exercise effective bacteriostasis and (g) are efficient as preservatives for the purposes for which they are recommended.

Antibiotics, being compounds of pronounced biological activity whose nature is only partly understood, should be used only under careful surveillance to prevent misuse and abuse.

Any permitted use in or on foods should be subject to repeal in the event that (a) their microbiological selectivity gives rise to new or "abnormal" spoilage or disease or (b) evidence for the significant increase in the prevalence of antibiotic-resistant pathogens as a result of their use in foods becomes apparent.

Antibiotics should be allowed only in foods where social practices would indicate cooking as the normal treatment for such foods and when cooking would destroy the antibiotic present.

Evidence available to date supports the view that in Canada the foregoing conditions are met in respect to the allowance of chlortetracycline or oxytetracycline as preservatives in poultry or in fish provided that the concentration of the antibiotic in any part of the food does not exceed seven parts per million in poultry and five parts per million in fish and provided that treated foods are clearly labeled to that effect.

Any abuse in the use of antibiotics or any attempt to overextend the shelf life of such foods in market practice will need to be subject to strict action by food-control authorities.

The use of antibiotics in foods should be coupled to increased effort to improve the practices of sanitation and hygiene related to the production, processing and marketing of foods.

The use of antibiotics as preservatives in foods should be considered as a tentative venture, since final conclusions on specific aspects of the sustained value and safety of such practice can only be determined after appropriate experience.

Each and every antibiotic proposed for use in or on foods must be considered on its own merits for the purpose recommended and in relation to its continued value in the medical field. **[The End]**

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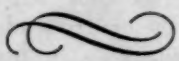

By NORMAN C. WRIGHT, C. B.

The Control of Chemical Additives in Practice in Great Britain in Regard to

RECENT ADVANCES in many branches of science and their application to food-manufacturing techniques have provided new opportunities to the food industry to improve its products—in appearance, texture and flavor; in maintenance of nutritive value; and in enhancement of keeping quality and the resulting reduction in food deterioration and wastage. In no branch have these advances been more rapid or more extensive than in the variety of chemical substances potentially available as intentional additives to food; it is right that, provided the interests and health of the consumer are safeguarded, advantage should be taken of their beneficial effects.

These advances have, however, presented new and difficult problems to governments and other authorities responsible for protecting the consumer against preventable hazards and the risks of deception. The purpose of this paper is to describe briefly the official machinery available for this purpose in Great Britain and the steps so far taken in this direction. I should perhaps add that I do not propose to make any reference to additives included in foods for the purpose of enhancing their nutritive value (for example, vitamins or minerals) or to accidental additions, such as residues of pesticides. The latter will be dealt with by my colleague, Dr. E. J. Miller, in the next paper.

Britain has a long history of food laws, dating back to the eighteenth century, designed to afford consumer protection. The most recent of these are the Food and Drugs Act, 1955, which applies to England and Wales, and the corresponding Scottish Act, the Food and Drugs (Scotland) Act, 1956. In general, these acts do not specify in detail what may or may not be done, but express their intentions in broad terms. For example, they make it an offense to add a substance to food so as to render it injurious to health or to sell, to the prejudice

in Food, Other than Antibiotics—
to Additives Intentionally Used in Food

This Conference Speaker—Chief Scientific Adviser (Food) to Britain's Ministry of Agriculture, Fisheries and Food — Describes Briefly the Official Machinery Set Up and the Steps Taken in His Country to Handle the Problems Involved in Dealing with the Subject of Food Additives

of any person, food which is not of the nature, substance or quality demanded. But whether these or other general provisions in the acts have been contravened is a matter for the courts to decide.

Such general provisions, while clearly essential as a basis for consumer protection, obviously require some supplementation in dealing with the complex technical and medical issues involved in the use of chemical additives. The acts, therefore, vest in the ministers concerned powers to make regulations "prohibiting or regulating" the addition of substances to food intended for sale for human consumption insofar as these appear to them to be "necessary or expedient in the interests of public health or otherwise for the protection of the public." Such regulations are, of course, subject to the over-all control of Parliament. They have the full force of law; infringement can involve the same penalties as apply to a breach of the acts themselves. As supplements to the general provisions of the acts, they are of advantage not only in being more quickly made and amended and in specifying in greater detail—based on authoritative technical and medical opinion—the measures necessary for consumer protection, but equally in providing clearer guidance to the local authorities (who are responsible in Britain for enforcement measures) and, by achieving a greater measure of uniformity, in benefiting the manufacturer who markets his products over a wide area of the country.

It is, however, clear that, in the exercise of such detailed regulation-making powers, the ministers concerned will tend to look for advice to some broadly based body which can examine the relevant evidence and made the necessary recommendations. In regard to regulations relating to food composition, the body set up for this purpose is the food standards committee, a committee appointed by ministers and containing members nominated by the Medical Research Council, the Association of Public Analysts and the food industry, as well as members appointed on a personal basis and officials of the government departments most closely concerned. The committee's recommendations are governed by the stipulation that they should be designed "for preventing danger to health, loss of nutritive value, or otherwise protecting purchasers." This committee occupies a central position in the field of food additives in that it has the ultimate responsibility for recommending measures for controlling their use. Its terms of reference are, however, extremely wide; they cover recommendations relating to food standards in general, as well as to the description and labeling of foods. In these circumstances, the task of dealing with the major groups of food additives was entrusted by the committee to a specially constituted subcommittee under the chairmanship of Professor Sir Charles Dodds. The membership of this subcommittee is drawn from similar interests to those of the main committee, there being some joint membership.

Early Regulations Relating Specifically to Food Additives

Apart from certain regulations restricting the use of mineral oil and of artificial sweeteners in food, the only legislative measures dealing specifically with the use of food additives at the time of the subcommittee's appointment were the public-health (preservatives, etc., in food) regulations, which had remained substantially unchanged since 1925. These regulations covered preservatives, coloring matters and certain miscellaneous additives, such as thickening agents. It is worth noting in passing that they employed a variety of methods of control—that of a permitted list (with stipulations as to quantities) for preservatives, a prohibited list for coloring matters, and a blanket prohibition against thickeners in cream. The great development in the production of potential food additives which had taken place since 1925 made these regulations the obvious starting point for the subcommittee's review—a fact which is clear both from the title of the subcommittee (it is termed for convenience the preservatives subcommittee)

and from its terms of reference, which charge it with the responsibility for reviewing the whole field covered by the regulations and, where desirable, making recommendations for their amendment.

It will be convenient at this point to say a few words about the working procedure, followed by the subcommittee and its parent committee and by the government departments concerned, in dealing with food additives.

Order of Subcommittee's Dealing with Additive Groups

The subcommittee decided, in view of the very wide field which its terms of reference covered, to deal separately and in the following sequence with the various groups of additives: first, antioxidants, since there was doubt as to whether the existing regulations allowed their use at all; then, coloring matters, for which the existing regulations appeared in most drastic need of revision; then, emulsifying and stabilizing agents (more succinctly termed, in the United States, "surfactants"), which constituted in many respects a novel field; and, finally, preservatives, for which there was already a limited permitted list and in which, therefore, the need for immediate action appeared less urgent.

The examination of each individual group of food additives commences with an invitation, widely publicized, to all interested parties to submit written evidence indicating those which they wish to use, how the additives will be used, and the advantages likely to accrue from their use. This information is supplemented by the collection of scientific evidence on both the technical and medical aspects and, particularly, evidence as to the possible effects of the use of the additives on human health. This latter aspect is not easy to assess. The subcommittee has no biological testing facilities at its own disposal, and there is a serious shortage of such facilities throughout the country—a situation which, until remedied (and proposals to this end are at present under consideration), must inevitably constitute a severe handicap to the rapid and adequate assessment of any health hazards. The subcommittee can and does make use of the results of work carried out in other countries, notably in the United States, and, of course, such results as are available from our own industrial laboratories. In passing, it might be noted that provision has been made in the present food and drugs acts for ministers to require the production of evidence of any investigations relating to health hazards by those producing, im-

porting or using substances included in any specified class of food additives, though the willing and voluntary cooperation of the interests concerned has never yet necessitated such statutory action.

Regulations Procedure—from Subcommittee to Parliament

On the basis of all the evidence examined (that relating to health hazards being assessed by a pharmacology panel comprising the medical members of the subcommittee, together with other experts) the subcommittee prepares a report summarizing such evidence and containing its specific recommendations. This report, after endorsement by the food standards committee, is published, and a sufficient period is allowed for interested parties to submit any observations on the recommendations to the relevant government departments. These representations are carefully considered and, if necessary, referred back to the subcommittee for further advice. Thereafter, when decisions have been reached by ministers, specific proposals for giving effect to them are circulated, thus providing the interests concerned (including, of course, the enforcement authorities) with a still further opportunity to comment. This may give rise to additional modifications before regulations are finally laid before Parliament. These wide consultations are felt to be essential in view of the complexity of the issues with which the whole subject abounds and of the need to ensure that everyone has a reasonable opportunity to state his case. They do, however, inevitably involve a considerable lapse of time before statutory effect can be given to the recommendations contained in any one of the subcommittee's reports.

Nevertheless, the subcommittee's six years of unremitting work have already resulted in substantial progress. The most notable advance is the making, just a month ago, of new regulations governing the use of coloring matters in food. In place of a *prohibited* list containing certain metallic and vegetable colors and five coal-tar colors, which was the basis of the earlier regulations, the new regulations embody a *permitted* list of certain colors of natural origin and of 30 coal-tar colors. Perhaps this comparison would sound more convincing if the fact were stressed that, as against the original prohibition of five coal-tar colors, the adoption of the permitted list has, in effect, resulted in the prohibition of the use of about 70 coal-tar colors which were submitted for the subcommittee's consideration. Moreover, such a permitted list will in future effectively prevent any other new and

untried colors from being used in food until they have been shown to be free from any detectable health hazard. In this connection it must be emphasized that none of us would claim that we have found the complete answer for all time. The evidence about many colors is still imperfect, the existence of conflicting evidence remains in some instances unexplained, and there are unresolved differences over the interpretation of results. It is clear that as new information becomes available, revisions may from time to time have to be made. But the principle of the permitted list has been accepted and a list has been approved which, we believe, meets the reasonable requirements of food manufacturers in this country, consistent only with the government's overriding responsibility to safeguard the health of the public.

Moreover, the subcommittee has made, and ministers have accepted, two other important recommendations: *First,* with one exception—citrus fruit (where special labeling is permitted as an alternative) —the use of coloring matters in unprocessed meat, fish, fruit and vegetables has been prohibited, irrespective of the harmlessness of the color. This is a good example of the use of a prohibition to prevent the consumer from being misled as to the "nature or quality" of the food purchased. *Second,* approval, in principle, has been given to the formulation of specifications of purity of the permitted colors, a task in which the government departments concerned have been fortunate in securing the assistance of the British Standards Institution.

Stages in Process Illustrated

Coloring matters are the first group of food additives to which the subcommittee's recommendations have been given statutory effect. The remaining groups form useful illustrations of the various stages of the technical and administrative procedures which I have already described. As regards *antioxidants,* a report containing the subcommittee's recommendations has been published, representations have been received and considered, and ministers have now agreed that certain specified substances should be permitted a limited use in this country. Regulations to give effect to this decision are in course of preparation. As regards *emulsifying and stabilizing agents,* the subcommittee's report has been published, a period has been allowed for representations by interested parties, and these representations are now under examination. As regards *preservatives,* the subcommittee is still engaged in its own review of the whole field. The problems involved

even with traditional preservatives are complex since, apart from any direct health hazard in the preservative itself and the possibility that it may adversely affect the nutritive value of the foods to which it has been added, there are considerations which impinge on the field of hygiene. There is, moreover, an added complication in that proposals have been put to the subcommittee for the permissive use of certain antibiotics as preservatives. Without entering into any argument on this point (which is to form the subject of this afternoon's discussion), I would only mention here that, in view of the importance of the issues involved, a special antibiotics panel has been set up and is at present engaged, in association with the subcommittee, in examining the medical aspects of the problem. The panel's advice will no doubt be embodied in the subcommittee's recommendations in this difficult and novel field.

Importance of International Cooperation

So far I have attempted in this paper to describe briefly the official machinery and the steps taken in Britain to deal with the problems involved in the control of food additives. May I turn now for a brief space to an aspect of the problem which goes wider than our own national boundaries, namely, the value of international cooperation in this field? I do this not only because of its obvious importance to all those attending this conference but because, since neither the World Health Organization nor the Food and Agriculture Organization of the United Nations could be directly represented here, they have asked me—as chairman of the Geneva Conference on Food Additives, in 1955—to refer to their activities in the international sphere.

The fact that there is only one synthetic color which is common to the permitted lists of all those nations which have such lists has, I fear, come to be looked on as almost a standing joke! I am personally not one of those who believe that we should necessarily have uniform regulations in every country; conditions in the undeveloped countries and, particularly, in those situated in the tropical regions are, for example, sufficiently different from those in Europe and North America as to make this neither practical nor desirable. But there is no doubt that we ought to aim at the maximum area of agreement. The advantages to international trade are obvious; less obvious, but perhaps no less important, are the benefits to be derived by governments if their decisions are based on the widest measure of agreed scientific opinion and their actions conform as closely as possible to those of other countries.

Need for Scrutiny of Reports Growing Out of Geneva Conference Studies

The approach which was adopted by the Geneva Conference was, in this respect, fundamentally sound. It sought to secure, first, the formulation of general principles which might appropriately govern the use of food additives and, thereafter, the formulation of suitable methods for the biological testing of such additives and for the interpretation of the results. These tasks were to be undertaken initially by expert committees, the members of which would be appointed on a personal and not a national basis. The reports of the committees would, it was hoped, thereafter be accepted, either in whole or in part, by member governments as a basis for their own national policies. This approach has been implemented to the extent that the two committees have now met. The report of the first has already been published; it is anticipated, I understand, that publication of the report of the second will not be long delayed. Both reports need to be studied critically and in detail by member countries, but it is to be hoped that in the control of chemical additives in food they will contribute—as will this meeting today—to increased international cooperation and, eventually, to a wide measure of international agreement. **[The End]**

• FDA REPORT FOR JUNE •

On July 28, 1957, the Food and Drug Administration announced 39 seizure actions against unfit food products during the month of June, but praised the food and drug industries for voluntary actions to assure the safety and purity of their products. Commissioner of Food and Drugs George P. Larrick said that FDA inspectors had reported 71 voluntary actions during June to improve sanitary conditions. One such project involved a $2 million food-plant renovation, which was launched following an FDA inspection. As a further result of the inspection, the company organized a school for its plant superintendents and sanitarians throughout the United States to teach them inspection methods used by FDA.

Mr. Larrick cited other examples of voluntary action. Among them was an improvement project by a leading brewery, which had a condensation problem involving the ceiling above open tanks where yeast was processed. An FDA man called the fact to their attention; the firm installed dehumidifiers, had the ceiling sandblasted and repainted, and put in three new sanitary-type pumps. The bill for the improvements totaled $12,140. As a result of a three-day inspection, another food-manufacturing establishment hastened to adopt 34 of 36 specific suggestions concerning practices in storing and handling of materials and equipment and also in its cleaning methods.

By E. J. MILLER

CONTROL OF CHEMICAL ADDITIVES

Practice in Great Britain in Regard

I SHALL RESTRICT my account to pesticides (a term which we interpret to include not only the usual chemicals but also such things as growth depressants, growth stimulants, defoliants, fruit-thinning and setting agents) and their use. The sale of the more toxic ones is controlled, as with other toxic chemicals, by the poisons rules.

Our present aim in Great Britain is to control by voluntary means rather than by legislation the hazards arising from the use of pesticides. To this end, we have an advisory committee, established in 1954, which is charged with the task of advising the government on *all* risks arising from the use of pesticides in agriculture and food storage. This committee (its full title is "Interdepartmental Advisory Committee on Poisonous Substances Used in Agriculture and Food Storage") was established as a result of a recommendation made by a working party—the Zuckerman Working Party—set up in 1950 to investigate these risks. Its first report dealt with risks to operators, its second with risks to consumers of treated crops, and its third and final report with risks to wildlife.

The committee consists of administrative and technical representatives from the government departments concerned with the problem, namely those of health, agriculture, fisheries and food, trade, and the government chemist. The medical and agricultural research councils and the nature conservancy are also represented. The committee looks to its scientific subcommittee for technical advice, as the latter body consists of experts chosen for their knowledge of subjects in this field.

The work of the advisory committee may be classified broadly under three divisions: "risks to the user," "risks to the consumer" and "risks to wildlife." It concerns itself only with agriculture and

OF FOOD, EXCLUDING ANTIBIOTICS–
to Pesticide Residues in Foodstuffs

Speaking at the July 26 Meeting in London, Dr. Miller—Chemist in the Plant Pathology Laboratory of the British Ministry of Agriculture, Fisheries and Food, at Harpenden, England—Describes Workings of the Government Voluntary Crop Protection Products Approval Scheme

food storage, and not with the use of pesticides in the veterinary or public-health fields nor with the biological effectiveness of pesticides. The effectiveness of pesticides for agricultural and horticultural use is a province of the voluntary crop protection products approval scheme.

Of the three types of risk mentioned, recent legislation has dealt only with that of the user. Apart from the general provisions of the food and drugs act, which provide an over-all safeguard for the consumer, control of the other two rests mainly on continued cooperation with outside bodies such as the pesticide manufacturers, agricultural spraying contractors and growers. The membership of the advisory committee and the subcommittee is confined to officials; liaison is achieved by means of panels of representatives from the subcommittee and interested organizations. To date, eight panels have been formed, dealing with topics such as residue analysis, organomercury compounds, antibiotics and arsenicals.

Briefly, the committee functions in this way: Information on a pesticide is collected and studied by the subcommittee. It is my task, as a joint technical secretary, to obtain and assemble the information on agricultural chemicals, my colleague being responsible for the stored products side. If the subcommittee considers the data to be adequate, it formulates a number of recommendations which go to the advisory committee, together with the supporting data. They are

required to be accepted by the advisory committee and by departments before going to outside bodies which have the opportunity of commenting on them before publication. They are then distributed on a wide basis. With a crop-protection product, copies go to the official agricultural advisory services, the National Farmers' Union, trade journals, the manufacturer's association, and so on. The latter —the Association of British Insecticide Manufacturers—represents over 90 per cent of such manufacturers in Great Britain; it cooperates closely by advising its members to include our recommendations on the labels of their products. Thus, the ultimate user receives the same advice, whether he reads it on the label of the product or in a trade journal or receives it from an agricultural advisory officer. A similar procedure is followed for a chemical used for the protection of stored products; in this case the appropriate trade organization is the Industrial Pest Control Association.

How Recommendations May Vary

The recommendations are usually set out under the three categories of user, consumer and wildlife risks. The Agriculture (Poisonous Substances) Act 1952, which is administered by the Ministry of Agriculture, Fisheries and Food and by the Secretary of State for Scotland, is concerned with risks to users. The recommendations may vary according to whether the pesticide is considered to be too toxic to be used at all by agricultural workers, in which case, under the act, its use can be banned, or whether it is sufficiently toxic that its use should be controlled by legislation, in which case—and after consultation with interested bodies—it is included in the regulations made under the act. Again, the chemical may be considered insufficiently toxic to require its use to be controlled by legislation, in which case voluntary precautionary measures are suggested and these are seen by the trade before publication. Finally, the chemical may be of such low toxicity that no precautions in its use need be recommended by departments. The protection of the user of fumigants such as hydrogen cyanide, methyl bromide and ethylene oxide on stored products is administered by the Home Office either by legislation (in the case of HCN) or by the issuance of voluntary advice.

If a chemical is named in the agriculture (poisonous substances) regulations, a workman must wear the stipulated protective clothing when carrying out a specified operation with it. At present, the requirements of these regulations are under scientific study by two

research workers at the plant pathology laboratory who are particularly concerned with inhalation risks.

Consumer Risks

Turning to the question of consumer risks: We have not hitherto felt in this country that we knew enough about the accuracy and reliability of methods of residue analysis to be able to recommend tolerance levels for residues in foodstuffs. The problem is being attacked at the government chemist's laboratory, where a small team of scientists are assessing published and unpublished methods of residue analysis for selected chemicals. The intention is to improve existing methods—and, if necessary, to devise new ones—to a stage where they can be submitted to collaborative examination and, having passed that test, to be published. Until we are able not only to fix residue levels, but to secure their enforcement, we are trying to achieve the same aim by advising restrictive conditions on the use of a pesticide. First we make it clear that we have no objection to the use of a chemical on a nonedible crop—one which is not consumed either by humans or animals. When used on a growing edible crop, one or more of three restrictions may be applied to a chemical; they are: (1) use on named crops only, (2) maximum dose per crop per season and (3) minimum interval between last application and harvesting. We believe that if these restrictions are observed, at the time of harvest the residue, if any, will be of such an order that, so far as our present knowledge exists, it is harmless.

The toxic nature of a chemical under consideration will determine whether all or some of the restrictions apply. Thus, with schradan, all three apply; with malathion, only the minimum interval is applied. The crops on which a chemical may be used are decided from a study of the residue data obtained following its normal commercial application.

Required Information

In general, comprehensive data are needed for staple articles of diet such as cereals, potatoes and peas; less comprehensive information may be demanded for foodstuffs, such as cucumbers, which are consumed in small amounts over much of the year, or raspberries, which are consumed in larger amounts for a short season. With a crop such as hops, which is subjected to a processing before consumption, the amount of information needed may be even less.

When crops are treated at the time of harvesting or during storage, information is required both as to the amount of the pesticide which gets into the crop at the time of treatment and its fate during subsequent storage and distribution. This applies, for example, to fumigants used on stored products, which are first sorbed and which may air off completely, break down or combine with a constituent of the product.

Voluntary Notification by Manufacturers

One recommendation in the second report of the Zuckerman Working Party was that a voluntary notification scheme should be devised whereby manufacturers notify departments of their intention to market a new chemical, a new formulation, or a new use of an existing chemical and that the agreement of departments as to the safe use of the notified product should be obtained before it is sold. Such a scheme has recently been agreed upon with the department of trade. It allows firms discretion when notifying, for they are required to notify only if a toxic hazard (or increased hazard in the case of a change of formulation) is likely to arise from the use of their product. The onus is on the notifier to submit evidence in support of a notification. To assist firms in deciding on the nature and amount of information needed in support of their notifications, two panels have been formed, to which experts come from both manufacturers' associations and departments, to draft broad guidance on the toxicological and residue data required. In addition, firms are urged to consult on an informal basis the officials who will be responsible for steering the notifications through the procedure outlined above. Firms are advised to notify as early as possible; for this reason notifications are mostly confidential so that after recommendations have been agreed to by departments, they go to the notifier only and are not published until the firm agrees that the matter is no longer confidential. Before the introduction of the scheme, notifications on an informal basis have been coming in for over a year and, based on that experience, we feel optimistic that the scheme will prove workable.

I have given you a brief account of the way we do things over here. Having heard it, you may feel inclined to agree with the concluding words, used in an American journal which described the voluntary crop-protection products approval scheme, that "only in Great Britain could such a Scheme work." **[The End]**

Antibiotics and Hazards

By A. L. BACHARACH, M. A., F. R. I. C.

This Paper Is Derived from the Conference Remarks of the Chairman, *Sous-Commission* on Antibiotics in Food Appointed by the *Commission Internationale des Industries Agricoles* and the *Bureau International Permanent de Chimie Analytique*

I PROPOSE IN THIS PAPER to tackle only two tasks. The first is to summarize, for the record, present legal position, insofar as I have been able to understand it, relating to the use in Great Britain of antibiotics for any purpose. The other is to enumerate what appear to me to be those hazards most deserving examination, from among the number that have been suggested as likely to be due to the presence of antibiotics in food for humans. I shall do little more than list these alleged hazards and perhaps try to separate those that an antibiotic shares with other chemical additives and residues in food from those due to its special properties.

I distinguish between food additives and residues not because the effects they have on any consumer are influenced by their way of reaching him, but because pragmatically it is easier to deal with an unwanted substance in a food if we know how it gets there. I call a "food additive" any substance deliberately incorporated in food for a specific purpose and intended to remain in the food at least up to the time it is consumed. As a "food residue" I describe a substance introduced onto or into a food plant or animal, or a food prepared from either, at any stage between its growth and its storage as a raw food awaiting cooking or processing, yet not intended to be present in significant amounts when the food is consumed.

[Editor's Note: At this point, Mr. Bacharach summarized ways in which antibiotics may enter foods, as a result either of current uses or of practical extensions of research, through presentation of two pertinent charts.]

In Great Britain, at present, only a limited number of the charted uses can introduce antibiotics into food, if only because a limited number of uses are permissible by law or can be practiced by agreement with the authorities. During a preliminary period from 1944 onwards, the uses of penicillin, and later of streptomycin, chloramphenicol and chlortetracycline, were controlled by a special penicillin act. These antibiotics and others were subsequently brought within the ambit of the consolidated Therapeutic Substances Act of 1956, which came into operation in that year. That act, together with the regulations made under it, is the administrative responsibility of the ministry of health.

Throughout, the aim has been—albeit for a number of different and changing reasons—to prevent the use of antibiotics by any but medical or veterinary practitioners; this is what the acts have largely achieved. It has involved the surveillance and licensing of manufacturers, as well as powers over distribution. It might also have appeared to make desirable some legal definition of "antibiotic," since it is hardly practical politics to amend an act of Parliament every time a new antibiotic comes into general use or an old one is discarded. However, the problem has been solved by a now well-established device, that is, by naming in a schedule to an act or in a regulation made under the act those substances that are to be held to fall under the act. This schedule can be quickly amended, whether by deletion or addition, through the placing before Parliament of statutory instruments specifying the nature of the changes.

When the value to young growing livestock of including some antibiotic in their rations under the normal conditions of practical animal husbandry became generally accepted, two antibiotics named in the relevant schedule—penicillin and chlortetracycline—were expressly exempted from the operation of the therapeutic substances act, provided they were being used in animal feeding stuffs under carefully defined conditions. This exemption can be extended, if desired, to other scheduled antibiotics, but such exemption is clearly unnecessary for any substance not mentioned in the schedule to the act, even though it has to be considered an antibiotic by origin and properties.

There is nothing, as far as I know, in British legislation about feeding stuffs to prevent such additions; therefore, scheduled antibiotics (with the exceptions noted) are, at present, absent from feeding stuffs (and so from foods) by a negative ban of the ministry of health and not by a positive ban of the ministry of agriculture, fisheries and food. Antibiotic substances not scheduled are absent because no one—at present—wants to put them in. This position could easily change, for nutritional or economic reasons, but the legal and administrative action needed to keep the position under control would be relatively easy to take.

When it comes to the use of antibiotics as antimicrobial agents for preserving food, a different mechanism is found in action. Since the Food and Drugs Act 1955 came into operation on January 1, 1956, a preservative (among other classes of food additives) cannot be added to a food unless it is mentioned by name in regulations made under the act. To recommend what preservatives may be used is the responsibility of a food standards committee; to accept (or reject) these recommendations is the joint function in England and Wales of the ministry of health and the ministry of agriculture, fisheries and food (and of the Secretary of State for Scotland). There is at present no permission to use any antibiotic as a preservative food additive; it therefore makes no difference whether or not it is scheduled under the therapeutic substances act. Thus, the use of a scheduled antibiotic for such a purpose would involve legislative action, albeit by statutory instrument, under two separate acts. This is doubtless an admirable safeguard for the health of the community, and particularly of the lawyers and politicians in it.

Regulations operative at the present time have the effect that 13 antibiotics cannot be made or distributed except under the provisions of the consolidated therapeutic substances act. They are bacitracin, chloramphenicol, chlortetracycline (Aureomycin), Erythromycin, neomycin, novobiocin, oxytetracyline, penicillin, polymyxin, Spiramycin, streptomycin, tetracycline and Viomycin.

Of these 13, three—and only three—may be used in animal feeding stuffs and concentrates, under strictly defined conditions; they are chlortetracycline, oxytetracycline and penicillin. The remaining ten are available solely through medical and veterinary practitioners; they cannot be sold to a member of the public except by a qualified pharmacist on a medical prescription, nor are they available in bulk to any

manufacturer unless he is himself manufacturing under license in accordance with the terms of the therapeutic substances act.

Outside of the 13, however, any antibiotic substance is freely available to anyone who can buy it or make it, and for any purpose whatever, provided always that in using it he does not fall afoul of other existing legislation in general and, in particular, of the food and drugs act and the fertilizers and feeding stuffs act. Naturally, he must comply with these acts in all respects, and also when he is making use of an antibiotic under the therapeutic substances act.

Loopholes and Other Problems

The present provisions raise some nice points. For example, Dr. J. H. Taylor has called my attention to what appears to be a loophole in existing legislation. He tells me that farmers today frequently feed antibiotic-containing feeding-stuff supplements to their stock at levels so high as clearly to be exerting a therapeutic effect. Such action is taken deliberately, and it completely defeats one of the main objects of the therapeutic substances act, to say nothing of its effect on the incomes of veterinary surgeons.

Again, what is the legal position regarding milk from cows treated with penicillin or streptomycin for the suppression of mastitis should a detectable amount of the antibiotic, however small, be present in the milk at retail sale? Is this an infringement of the law concerned with liquid milk in Great Britain, which lays down that it is illegal to abstract anything from, or add anything to, milk sold for direct consumption? or is it covered by the principle of "appeal to the cow"?

Our legal colleagues might also like to give some thought to the problem of nisin, an antibiotic prepared from suitable strains of group-N lactic streptococci and increasingly used by cheese makers to suppress the growth of unwanted microorganisms, particularly certain clostridia, that can cause serious spoilage of both fresh and processed cheese. Nisin is not an antibiotic under the therapeutic substances act; neither does it appear to be a preservative under the food and drugs act. It is difficult to see what difference there is in principle between using nisin to prevent undesired bacterial spoilage in curds and whey during cheese-making and using tetracyline to prevent undesired bacterial spoilage in whale carcasses before processing. But in Great Britain the first is legal and the second, as far as I can make out, is not, though both are useful and both equally free of risk to the public.

Another problem is posed by Lotatin, a substance that can hardly fail to be considered an antibiotic by any reasonable assessment. It happens to be an oxidative enzyme able, in the presence of glucose and catalase, to deoxygenate closed containers. It is being found practical for use in preventing the oxidative deterioration of canned and bottled fruit. What is it—an antioxidant, a processing agent, a preservative? The only thing I can say for certain about it is that it is not a coloring matter—and probably not an emulsifying agent. But it would be interesting to know whether its use is legal—or merely connived at—and for how long it is likely to remain so.

The third main use of antibiotics to which I must now allude is as pesticides in agriculture and, more especially, in horticulture. In this country there is no legislative bar to the use of any substance on crops. But the pesticide manufacturers have always realized that it could hardly be to their interests to poison the public with copper and arsenic and organic phosphorus compounds as an alternative to their being killed by food shortages or by the consumption of decomposing animal and vegetable tissues, even if the ministry of agriculture were to remain supine while they did it. So it is that there exists a "gentleman's agreement" between the manufacturer's association and the ministry whereby nothing is used as an agricultural pesticide until agreement has been reached between them about its nature, formulation, and mode of administration. Even when this has been done, recommendations—often difficult to arrive at—are needed from the food standards committee as to the residual limits of the pesticide to be tolerated in specific edible crops; but, here, only two different sections of the same ministry—and not two different ministries—are involved, so that the need for strategic disentanglement is correspondingly less likely to arise.

Before the admission to use of a new additive, or residue-producing agent, there is a condition, besides those of safety and utility, that should, in my view, be made. I expressed this view at Amsterdam two years ago and am pleased to find support for it in the just-published FAO/WHO report of its expert committee on food additives. The condition is simply that either the manufacturer or the intending user (or both) should supply the essential particulars of an analytical method capable of establishing the presence or absence of the antibiotic in the foods involved and under the proposed conditions of usage. If the manufacturer (or user) does not possess this information,

he is not a suitable person to handle the antibiotic; if he does, he should be willing to hand over the information.

In spite of the complexity of the situation—and the further complication introduced by the fact that on the toxicological aspects of the matter another more or less independent government organ, the medical research council, has also its words to say and its part to play —it is only fair to add that the various officials who have to cope with one aspect or another of the situation do so in an enlightened and cooperative way and show great skill in not discouraging the enterprising manufacturer and in simultaneously protecting the public. On more than one occasion, they have foreseen complications arising and have of their own accord brought together all the parties likely to be involved if some particular scientific advance were to be embodied in technological practice. It is understood that at the present moment two of these advances—the use of antibiotics in meat and fish preservation and the use of antibiotics for the protection of fruit and flower crops—are the subject of intensive study in the departments concerned, with the object of minimizing delay between receiving applications to practice these new processes and taking the necessary decisions on whether—and, if so, how—they shall be employed.

What, then, if any, are the hazards arising to the public from the frequent, or even continuous, consumption of foods containing small residual quantities of antibiotics or small additive quantities used as preservatives? Many of the apparent objections raised apply equally to the use of any preservative other than one that is entirely nontoxic to man and yet also is indiscriminate in its bactericidal action. No such preservative is known or is likely to be. There is, in fact, always a risk that any preservative will encourage the growth of undesirable organisms by selectively eradicating competing species. The same kind of argument was used against pasteurization, but has been found insubstantial, provided that measures to increase hygienic practices in the dairy industry went *pari passu* with the technological attack on both pathogens and spoilage organisms. At best, the plea seems to read: "Please leave us our food spoilage organisms as 'tell-tales' for the presence of pathogens." I suggest that this is not good food technology; I doubt if it is even good bacteriology. Certainly, it is atrocious world food economy.

As to toxicity, including carcinogenicity, I think I need say but a word or two, although I have no intention of trying to define

"toxicity" any more than I did "antibiotic." Antibiotics are not toxic substances at all in any sense useful for purposes of food and drug law today. Such direct ill effects as have occasionally attended their use have all been from the relatively large and repeated doses given with therapeutic intent, and almost always by injection, at that. Ill effects from oral treatment have been still less frequent—hardly surprising, since the antibiotics with peptide structure are unlikely to escape intact from gastric and duodenal hydrolysis and many of the other more commonly used antibiotics are poorly absorbed from the alimentary tract. If these substances are toxic, so are acetylsalicylic acid and Epsom salts; excess use of either of these useful drugs for overlong can lead to end results hardly less deplorable than those caused by strychnine or carbon monoxide.

Even the most terrified carcinophobes have not yet suggested that any antibiotic is by any route capable of evoking tumors in any animal, and we may leave this particular hazard for future consideration; neither can we at present assess the relevance of a so-far incomplete and somewhat vague report from Westergaard, in Denmark, to the effect that some antibiotic has shown under some conditions some mutagenic action on some organism. This does not necessarily make polymixin, say, any more dangerous than formaldehyde.

I come, then, to the questions of allergy and drug-resistance. The ability to evoke these responses is, it is urged, not characteristic of any other group of food additives or of any known food residues, but is highly typical of antibiotics, and so demands special wariness over introducing them into human foods. I do not propose today even to begin to discuss either of these highly complex biological phenomena. Even if I were competent, I should not have the time. Yet we should note certain facts against the background of which I suggest that these somewhat sinister warnings must be assessed.

We know, from carefully collected results on both sides of the Atlantic, that an appreciable percentage of the population, for several periods in the year, is daily consuming quantities of milk containing detectable quantities of penicillin and, possibly, also of streptomycin or some other antibiotic, present as a residue from the individual or herd treatment of cows having mastitis or thought likely to be at risk. The number of these involuntary and unconscious penicillin eaters must by now have run into many hundreds of thousands. No single case of consequent ill results has so far been reported. The residual quantities are known to be small or even minute, and the

antibiotic present is subject to destruction by heat and digestion, among other factors. I, for my part, am satisfied that the present levels of use involve from this source no risk at all of evoking an allergic response in the casual consumer or of causing him to harbor strains of antibiotic-resistant pathogens or other undesired micro-organisms.

In passing, I would remark that at least two of the risks of which some have warned us balance one another out. The one I have just mentioned is the build-up from successive low-level bacteriostatic doses of drug-resistant pathogens. The other is the possibility that the so-called decomposition products of an antibiotic, produced during processing or digestion, may be toxic, even though the antibiotic is not. What is certain, however, is that these decomposition products will not be bactericidal or even bacteriostatic. At least the consumer of antibiotic residues or other breakdown products will not have to face both the alleged risks simultaneously.

Finally, a word about possible allergies: There is no doubt that a few individuals—in relation to the total treated, an almost insignificant number—have an abnormal sensitivity to certain antibiotics, notably penicillin. Apart from occasional incidence among factory or hospital workers handling antibiotics, there is no record of an allergic reaction to penicillin or other antibiotic having been evoked by levels of dose or routes of administration other than the therapeutic. The chances of a sensitized person meeting in his food the right antibiotic in the right quantities and under the right conditions to evoke in him serious allergic responses seem to be infinitesimal, nor is there the slightest evidence that anyone has been sensitized to any antibiotic by ingesting the minute quantities of it occasionally to be found at the present time, residual in milk or other foods, such as broiler fowls in North America.

Nevertheless, the position should not be regarded with complacency or even with indifference. The truth is that there seem to be serious gaps in our knowledge, although I am not among those who believe that this need stand in the way of intelligently planned technological advance. But we do not appear to know what are the smallest oral intakes of any of the antibiotics that can evoke an untoward response in previously sensitized individuals—whether the allergy is innate or acquired—nor have I been able to find information about how small an amount of any antibiotic by the oral route can produce sensitization. The same is true about the degree of skin

exposure, as—for example—in a factory or dispensary. Experience to date, however, strongly suggests that both the sensitizing and the evoking doses must be far below the amounts that there is the remotest chance of encountering in foods produced by any practiced or projected process. All the same, it would provide useful knowledge—and, I believe, added confidence—if we could have quantitative experimental results as data on which to base realistic limits of tolerance for antibiotic additives and residues in our foods.

Does Allergic Subject Really Warrant Protective Legislation?

In any event, let me leave you with a simple issue to consider: Is the allergic subject a matter for legislation at all, except in the sense of securing by law that he, like everyone else, can get proper medical attention? What can any parliament do about children allergic to milk protein and adults allergic to strawberries or shellfish? Can we ever legislate, other than in the most general terms, to protect the millworker from flour dermatitis and the miner from coal dermatitis? It is unlikely that we shall decide in their interests to prohibit the use of coal and flour and milk—or even of scampi. Surely these individuals create problems not for lawyers and legislators, but for the medical profession—both because of their rarity and because of the special treatment they demand. May I perhaps conclude by modifying a Latin tag that must be well known even to some of the chemical members of this audience: I suggest that *"de allergicis non curat lex."*

I wish to express my gratitude to a number of colleagues, at home and abroad, for information—which I hope I have transmitted correctly—and for opinions—which I hope have served to curb my own worst illogicalities and extravagances. I am particularly grateful to D. C. M. Adamson of Glaxo Laboratories, Ltd., and also to Dr. W. F. J. Cuthbertson of that firm; to Dr. J. H. Taylor of Cyanamid Products (Britain), Ltd.; to Dr. Bernard L. Oser, of Food Research Laboratories, Inc.; and to the other members of the international *sous-commission* on antibiotics in food for their discussion at its Como meeting last May. Need I add that, as the *sous-commission* has not yet reported, none of the opinions expressed in this paper are to be attributed to them, even the sound ones, and that I alone am responsible for the views I have been expressing and the presentation of the facts I have tried to set down? **[The End]**

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That you spend too much time getting too little information is true of a great many of the tests which are carried out in this field and, again, I think that the research might very well be put back into the proper background of food research as a whole. One of the things that I think is holding up the food technologists is the lack of information about the general material. I think that food research needs to be sponsored on this particular study of the subject we are discussing this morning.

"The second point has already been touched upon, but I would like to underline it again. If you are going to have tolerance levels, I think it is fundamental, if I may say so with great respect in the presence of lawyers, that you cannot do that unless you in fact check them and enforce them. It is therefore a question of fundamental chemical analysis, perhaps not direct but some assessment of the treatment that has been used. If we have these tests, and I am sure they can be devised, it is important that the substance which is in fact used in food should be the substance which in fact was tested. There is in fact at the moment no satisfactory guarantee, because there are no specifications of the substances which are tested and approved.

"It seems to be something essential. It was found essential in the drug field, and there is no reason why it should not be in this one.

"Finally, there is one other point. On the question of the flexibility of these regulations, there is a real problem here, I believe, that when a food is introduced, especially on a tolerance limit basis, on the basis of some specific use—as I think you mentioned at the very beginning—it is possible for this use to change, and it is possible for a substance introduced, shall we say, for the treatment of some food A, for some of it to be found very useful on food B, and C, and other foods. This I think demands some thought. It is a real problem, and one which obviously demands considerable flexibility in the administration of any sort of regulations which are provided.

"The CHAIRMAN: Dr. Wright, I will ask you to respond first to this question.

"Dr. Norman C. WRIGHT, C.B.: It would hardly seem to me that this question needed any response. It would seem a very useful contribution from Mr. Frazer, who has such wide practical experience. He said himself, with regard to his first point, that he has recently served on the joint W. H. O. and F. A. O. panel, and has himself therefore contributed towards the field in which I know we all seek help from as many and informed sources as we can get.

"On the tolerance levels he did raise the question of the identity of the substance in the food, and with regard to the United Kingdom I mentioned in my paper that we were looking into this in regard to specifications of purity which, I hope, will also have with them specifications of identity.

"Finally, there was the question of flexibility in permissive use. I think in the United Kingdom so far as we can we are allowing for flexibility in the sense that we are doing most of this work by regulations which can be altered at the will of Parliament fairly rapidly.

"The CHAIRMAN: Mr. Harvey, will you kindly respond to that question and answer?

"Mr. John L. HARVEY: I think I too am in a happy position of agreeing with everything that has been said.

"I will come in only on the flexibility point. Taking as an example our Miller Pesticide Amendment, we have several—I think about 90—basic applications for the use of this or that pesticide on a particular crop or half a dozen crops, and those are constantly being amended. The amendment to the regulations is relatively simple; it merely involves supplying data as to the amount of residue and with respect to the addition to the crop, so I agree that it is entirely imperative that these be quite flexible, but I might say with our experience we have had no difficulty in keeping it sufficiently flexible. As soon as the addition is verified as having value, we have been able to amend to broaden the use quite a lot.

"Dr. J. Hubert HAMENCE: Mr. Chairman, ladies and gentlemen, arising out of this matter of analysis, now we have those schools of thought here I would just like to put a general question.

"I am very disturbed and alarmed, sincerely, when I hear from Dr. Miller that our methods of analysis in England are still so unsatisfactory that we are unable to make a recommendation to a limit for what may be a very potentially dangerous substance.

"On the other hand, the Americans have laid down their methods of analysis and they seem to have found it satisfactory to give a reasonable measure of control. I would like to put this question to the Americans. Have they found these methods of analysis which we all agree are to a certain extent approximate for residues? Have they found that satisfactory? Do they really think we want far more accurate methods of analysis?

"To the English side, I would put the question why they hold up to get this extreme accuracy in a matter which may at any time be a matter of life and death to quite a large number of people? I say that because the Ministry seem to be satisfied with the belief that if you give directions to a farmer as to what he shall do, you are all right. With my experience of farm hands I think they could not care less how they spray. They have no fear. They work amazingly well, but where a toxic substance is concerned, you can tell him it is a deadly poison and a fellow will take out a sandwich after using it and eat it. They are the most sincere people, the most hard working in the country, and they have very little fear of poisonous substances, yet we seem to rely on them.

"I am sure that our methods of analysis are not quite so dumb, and I would like to hear both sides of the picture.

"Dr. Eric J. MILLER: Mr. Chairman, I deliberately held up earlier on, and if Dr. Hamence is to get a full answer to his query you are going to be here until 2 o'clock.

"Quite briefly, on this point about the agricultural workers chucking the stuff on and then taking a sandwich out of their pockets is looked after in this country by the regulations governing the use of it. So far as the use of it by the consumer is concerned, I would point out that a long investigation was carried out by the Zuckerman party which came to the conclusion that no-one had died from eating treated foodstuffs and that the risk is not very great of dying from an acute dose. The risk, if there is going to be one, is from a chronic dose, over a long time. It is going to take a long time to evaluate that. If we are going to wait for that before allowing the use of the chemical, we might as well pack up and go home.

"There are two schools of thought about the methods of analysis. One school says, 'Put down the figure and leave the chemist to work out a method of detecting it.' The other school of thought says, 'We won't put down a figure until we know that that figure can be detected.' It has already been made clear that in developing a new chemical the onus, whether it is in the

United States or here, is on the manufacturer to provide details of a method of analysis.

"If I may take a specific case, there is one chemical in considerable use in this country now for which no known chemical method of analysis exists. It is a chemical which has not yet been in use in America. That particular chemical is a pesticide and—this is the point that Professor Fraser made —starts off as a mixture of two distinct chemicals. When it gets into the plant, as far as we know, and the research is still going on, it appears in two at least or three, if not more, toxic forms or derivatives, or whatever you like to call them. A method therefore has to be worked out for detecting each of those toxic derivatives. There is no method, as I say, yet but we are having a go in this country. But the manufacturer, in submitting his notification, was able to supply data based on the use of radioactive material. We developed a very specialised method in support of the notification, but that method is not applicable to the commercial product because that is not radioactive.

"If we are going to wait for a chemical method of detecting that particular chemical so that it can be used in this country under the system which exists here of the Public Analyst doing that sort of work, that chemical will not be in use yet or, probably, for a long time. So there are two schools of thought—either put the figure down and let the chemist work it out afterwards, or wait and let us satisfy industry and Government that the method is applicable, can be followed in different laboratories under different conditions, and still get the correct results.

"These then are the two schools of thought, and the one we are following at the moment is the second.

"Dr. Bernard L. OSER: I think it would be of interest to this audience to recall a statement made recently by a spokesman of the National Agricultural Chemical Association. He reported that currently the cost of developing analytical methods for the determination of pesticide residues has exceeded the cost of the toxicological work to establish a basis for their safety.

"The need for precision in analytical methods arises out of the establishment of tolerances, because it is no longer a matter of whether the amount of the pesticide is harmful or not. Our Food and Drug Administration has only to establish that the amount of residue is above a permitted tolerance level. Therefore the analytical precision required is quite great. Recognition of this problem was given at a recent meeting in Como on Foreign Substances in Foods. It was the third of a series of symposia sponsored jointly by the International Commission for the Agricultural Industries, and the Permanent Bureau of Analytical Chemistry of Foods and Drugs of which Professor Shabetai is scientific advisor. The International Union of Pure and Applied Chemistry in Paris last week appointed an ad hoc committee to explore the role that the International Union might take in this problem of food additives particularly from the point of view of the chemist.

"The CHAIRMAN: Mr. Harvey, do you want to add to the discussion?

"Mr. John L. HARVEY: I have one comment. I think that the precision and method of accuracy is required, primarily related to the toxicity of the substance, of the quantity of tolerance. If it is in tenths of a hundred parts per million, if it is 50, 100, 500 parts per million we have difficulty with the precision in the question.

"The CHAIRMAN: I would like to add two comments to those of Professor Frazer's on what you have said.

"In commenting on the proposed amendment of the Food and Drug Act with respect to food additives, speaking for the food industry one of the suggestions we made was that as fast as they are known the F. D. A. should be required to publish the methods of analy-

sis which they use, so that we shall all have the same rules of scientific analysis to follow, otherwise we shall achieve different results.

"Of course, we recognize the fact, as Mr. Harvey has emphasised—and will emphasise in his testimony before Congress soon—that new methods have to be devised constantly for new additives, and they cannot be published in advance, but they should be published as soon as they are known so that we shall have the same facts.

"My second comment is that our food industry is becoming greatly scientific. We have research folk and scientific folk in the industry who are constantly working on these problems of methods of analysis, and their applications. In addition to that our University campus are working on the problem, and the F. D. A. through its wonderful scientific group is working on these problems of methods of analysis, and the agricultural O. I. C. is constantly publishing monographs in those areas. The accumulated effect of these things through the scientific publication of papers is to provide universally the knowledge that you are anxious to have and which, of course, we must have in order to deal with this subject practically.

"The third comment I want to make is that in the United States we have an entirely different philosophy Government from that which prevails in Great Britain and Canada. In this respect, that we do not have these orders in council and effective regulations—administrative regulations—which are beyond Court review. In our country we believe in objective rules of conduct, and then their enforcement by the Court subject to adequate penalties. We do not like the notion of being required to go to the Government and get permission to do anything in advance. We just want to know what the rules are, and we want to assume the responsibility ourselves in complying with those rules, but in this instance we are leaving that traditional position, and we are approving the plan for the food industry of having the Government, through administrative regulations, sanction what we propose to do, if it is right.

"That is a historic departure in the food industry. We have had it in the drug industry through the new drug procedure, and in the field of biological drugs, as you know, and generally through the social structure of the drug law, but not in the food law, with some exceptions like the meat inspection act. It was with great reluctance that we in the industry came to the conclusion that we would agree to this form of advanced Government regulation before we could do anything, but we have agreed to it because we think in the balance the public health interest is paramount here, and should be thus secured. But we only agreed on the basis that we shall have three fair routes of review, if the administrator goes wrong in our opinion. First, the scientific review, which is a new thing developed to the Miller Pesticides and F. D. C. I. amendment, where on the request of a person or a manufacturer adversely affected by an administrative decision the National Academy of Scientists appoints an ad hoc impartial scientific referee committee to which we can go—the Government on one hand and we on the other—and submit our evidence. That committee makes the report to the Government, and if that report is against the Government, it is highly improbable that it will go contrary to it.

"On the other hand, if it supports the Government, we should probably have to take the position that we are wrong. So that scientific review is one of the most important reasons why we have agreed on the administrative control of chemical additives in advance.

"Then there is the administration in public hearing, where you rehash all the evidence and make all your evi-

dence, and if we can secure adjustive administration procedure through having a proper impartial hearing, we shall be satisfied.

"So far as the final review before the Court is concerned, we are advocating that that review be again a highly impartial one, although we are confronted with the administrative procedure in our country which provides at the present time that if the findings of the administrator in fact are supported by substantial evidence from the record, taken as a whole, then the Court must accept those findings. We have suggested the matter that although the Government does not agree with us, the findings should only be accepted by the Court when supported by the weight of evidence instead of by any evidence. Does that clear some of the problems in your mind? Have you any other questions that you would like to ask?

"Professor A. C. FRAZER: I would like, if I might, to ask a question about what Mr. Harvey said on this question of flexibility. Does he mean that the flexibility is much easier for a pesticide, because here you have the case that the manufacturers are responsible. In the other case, the manufacturer may cease to be responsible, and the food industry may do it without the knowledge of the people who made the substance. It is a different problem, perhaps soluble in the same way.

"The CHAIRMAN: The next questioner is Dr. Eric C. Wood, Public Analyst.

"Dr. Eric C. WOOD: I want to come back, if I may, to this question of methods of analysis by citing an example of something that actually happened a short time ago.

"A field of runner beans which were being grown under contract for a firm of processors had been sprayed with a spray originating from Germany. In this country the recommendation is that 6 weeks should elapse between spraying and harvest. In Germany the recommendation is 3 weeks, and those instructions are printed on the label. Unfortunately therefore this field of runner beans was sprayed 3 weeks before the expected date of harvesting. The processors, as soon as they heard of this, refused to take the beans because, they said, they could not take the risk.

"I was therefore approached, and asked if I would examine the beans and say whether they were fit for human consumption. In the first place there was no method of analysis that was either sufficiently accurate or speedy that was known to me. You will appreciate that the analysis could take 10 days or more to produce a result and the beans would not be worth much by then anyway. In the second place, even if I had been able to determine the amount of spray in the beans, there is no regulation in this country as to what particular tolerance would be allowed on the beans.

"The question was insoluble. They both thanked me, and I had a feeling that my prestige suffered considerably with the processors and the growers, and I discovered that the beans had been sent to Norwich Market where they had been sold in the ordinary way by retail.

"I do not know what the moral of the story is, except that we do want methods of analysis which are speedy, if not very accurate, and a tolerance that has one official or semi-official recommendation so that everybody can agree to work to it. It is not a question of merely saying that in the meantime we want to prevent somebody unknown from being ill, in some indefinite way. What we have got to deal with are these very practical problems. There is the problem like this one of the contract, and the query may be someone asking, 'What shall we do with this crop?' There may be £5,000 at stake. It is a very practical matter, and I want to emphasise that point.

"Secondly, if I may before I sit down I would like to go to the point about animal testing raised by Professor Frazer. I hope I would not be one of the people he would ask to sit down and shut up about these tests. I do appreciate the difficulties; you cannot make the manufacturer spend a lot of money in impracticable tests, but it does not follow that because a thing is safe for species A and B, it will be safe for species C, or homo sapiens.

"I have had that brought to my notice recently by some work from which it would appear that a feeding stuff to which an additive has been added, fed for a long time without any harm whatever to one species of poultry, apparently kills another species of poultry. You would have thought that two species of poultry are very closely allied, but the point seems to be that one species accumulates it and the other excretes it. Metabolically they differ. Again, what is safe for rats and dogs nevertheless may not be safe for human beings. I do not know what you are going to do about it. I just want to point out that the risk is there.

"The CHAIRMAN: Dr. Miller, would you like to make a comment?

"Dr. E. J. MILLER: I think Dr. Wood has partially answered his own question. He quotes the use of a product from Germany used on runner beans when the recommendations in this country say 6 weeks and in Germany 3 weeks. If he is talking about the same chemical that I think he is, the answer is that we have not made any regulations to the use of this chemical on runner beans, and therefore we hope —quite naturally under the present voluntary system—that it is not used on runner beans!

"Even if it were used on runner beans, even if we had a law in this country which said it must not be used on runner beans—and that in effect is the law in America, that unless it is a named crop you must not use it on that crop—and it is used in this country on runner beans, surely in all countries you are not punished for breaking the law, you are punished for being found out. There is nothing to stop this person sending the stuff to market in this country, except for the fact that the Food and Drugs Act—and I stand open for correction here, and perhaps Dr. Wright will answer this part of it—does give the overall protection to the consumer in that if that crop were taken and analysed and found to contain something harmful, then action can be taken.

"Dr. Wood then went on to say that he does not know a method of analysis, and a method could have taken 10 days to produce some sort of result. That is just my point. What is the good of putting down any tolerance if you have not got the method of analysis? So until we have methods of analysis we will not feel justified in trying to enforce a tolerance which is purely a paper figure.

"The CHAIRMAN: Dr. Wright, would you like to add anything to that?

"Dr. Norman C. WRIGHT: I do not think so, sir.

"The CHAIRMAN: The next slip bears the name of Mr. N. Goldenberg, of Marks and Spencer. He would like to join in this discussion.

"Mr. N. GOLDENBERG: Mr. Chairman, there are two points on which I would like information. One is addressed to Dr. Wright, about preservatives, and it is this. He made the point, as I understood him, that there would be a considerable amount of delay in publication of the recommendations of the preservative sub-committee, which we fully understand. But there are a number of individual items which have been submitted to their judgement for which I think they could express a view without delay. I in fact contacted them on one such case myself.

"There it seemed to be a fairly clear-cut case where the American legislation had already passed this chemical as an anti-mould preservative, and in this country we still await a decision. While

we fully appreciate that there must be delay for complete consideration it does seem to me that there is a case for publishing not the full list perhaps, but one or two interim lists of those chemicals which are known to be safe, or of which there is a good deal of experience and which have in fact been approved elsewhere by what I would call generally agreed competent authorities.

"I would like Dr. Wright to indicate to us whether such a device is feasible in order to obviate a period of delay which may extend even perhaps to a couple of years.

"The second question I have in mind I really address to our visitors from the United States. It is in connection with the possibility of food being contaminated by chemicals which are not added, but which are as it were deposited on them by means of what are called 'space sprays'. We all know that there are certain devices on the market which blow out a kind of aerosol which contains DDT or lindane in an effort to keep out flies and wasps from food processing premises and which, in the course of doing so, also deposits a certain amount of DDT or lindane on the ceilings, walls, floor and, incidentally, on any food which may be about, and any equipment which is subsequently used in manufacture. I believe I am right in saying that there is a report published by the American Medical Association which regards this practice rather adversely, and which limits it in certain ways, and particularly states that it does not recommend it for premises where foods are being processed.

"As we have here a number of distinguished experts from the United States of America I would very much like to hear their views on this matter, and also the views of the speakers from the U. K. who can give us an opinion on this matter. I know I am raising a subject which is somewhat controversial but as it is an important point I would be very glad to hear some views on it.

"The CHAIRMAN: Dr. Wright, will you respond?

"Dr. Norman C. WRIGHT: The first question Mr. Goldenberg asked was about the possibility of avoiding delay in regard to the agreement to using certain specific preservatives. The reason why the preservative sub-committee has not, so far as it can avoid it, given views on any individual substance within a group of additives is that it has preferred to examine the principle first and then deal with the individual instances on the basis of the principles established.

"There is a risk that if you look at one or two or three individual chemicals and give for instance permission to use those, then you establish a precedent. If you do not, equally you may establish a precedent. That is the first reason I think why the committee would be unwilling to give an interim view.

"The second point that Dr. Goldenberg raised in this connection was why should not such preservatives be used if they had the agreement of the United States authorities? With the greatest of respect to the United States authorities I would point out that in this country the interpretation of the preservative sub-committee has not always agreed with the interpretation of the Food and Drugs Administration, and that is very noticeable in the case of our colours list. It would not be possible for any body of advisers in this country to recommend a substance because an authority in another country had taken that course.

"There is already a limited list of preservatives, so this subject is at least partially covered. It would be possible for any individual interested to ask the preservative committee to deal with a substance in isolation, and the committee would then have to decide whether it did so, but I would point out that if the committee decided to do so and if it happened in a number of cases, it would put back the whole consideration of the general subject to preservatives and would therefore in fact be against

the interests of a considerable number of manufacturers of preservatives who wished to place their products on the market, but who were not asking for special priority.

"The final answer therefore, sir, is that there is no objection to any individual firm or interest approaching the preservative sub-committee, but I think we must leave it to the preservative sub-committee to decide in the general interests of the industry and the manufacturers to take something in isolation or leave it until they can consider the whole matter.

"The CHAIRMAN: Now I will ask Dr. Oser to respond to the second point.

"Dr. Bernard L. OSER: I am quite sure that the legal position with regard to a residue deposited on foods as a result of spraying food processing plants would be treated in exactly the same way as spray residues deliberately applied on crops. The question is not how it gets into the food, but is it there? For this reason the choice of sprays in food plants has been very carefully considered so that if it is likely to leave any residues on foods it is a permitted residue and within the permitted tolerance limit.

"Dr. E. J. MILLER: And now that the chemist has explained the legal position to the lawyer! Sometimes the legal position is not precisely the one carried out. We have had reference made to incidental contamination of pesticidal sprays, and Dr. Oser is quite correct in saying that as a pesticidal spray it must be approved in the sense that a tolerance has been established for it, for the particular food on which it occurs, otherwise it is, per se, a deleterious substance for spraying with regard to quantity.

"I believe that in the reference that I made this morning to the problem of contamination such as in agricultural products—such as market milk—with rather a fancy aggregation of pesticidal residues which are quite new but nevertheless are concerned scientifically if not yet legally, I pointed that out to distinguish between the legal position and what is being done. We do know that pesticidal residues are carried over onto agricultural products through contamination such as the spraying of cattle backs and so forth, and as yet we are developing a decision as to what can finally be done about it. Of course, if these residues are present in any quantities that represent a provable hazard we can move immediately by the various sanctions of the law, but it is a problem and it is a growing one. As we get more and more poisons, even in smaller and smaller quantities, we are confronted with the problems of allergistic and booster action, and additive action and so forth. It has become much more a matter of what is allowed by the law.

"The CHAIRMAN: We have now concluded the questions that have been submitted from the floor, and the time has come to adjourn this session. In closing it we have completed our discussion on the basic problems of the control of chemical additives in food.

"What is there that we should say in conclusion? Is it not true, ladies and gentlemen, that we are dealing with a common problem of public health that basically does not differ in your country or in ours, or in Canada? It is a question of protecting our people from the consumption of harmful chemical additives. We will differ between ourselves as governments in the kind of law that we will develop in the control of chemical additives, and as Dr. Wright has pointed out we will differ even in the scientific area as to the cause of the difference between the scientists on the solution of these scientific questions. We each have a different pharmacopoeia and different methods of analysis, but I think Dr. Wright made a basic point when he argued that while all this is true—the differences in our legal procedure and our legislative procedure, and in our scientific approach

and conclusions—nevertheless, we shall all benefit by trying to reach as near a common opinion on these problems as we can from the general standpoint, and that we can best do so by our common discussion.

"I therefore hope that you feel that by bringing together, as we have this morning, all of us to join in discussion we have educationally secured better knowledge of our subject and, I hope, a better understanding of how to solve the various problems which have been recited.

"With these remarks I conclude this meeting."

—Afternoon Session.—The afternoon session of the joint conference ended with the following floor discussion, reproduced in full text:

"Chairman: Sir Harry Jephcott

"The CHAIRMAN: Mr. Bacharach has mentioned in his paper Dr. Bernard Oser, who is here and wishes to take part in this discussion. I think he has something rather more than the ordinary things to say and so, Dr. Oser, if you will please come forward, we will give you 10 minutes.

"Dr. Bernard L. OSER: Mr. Chairman, ladies and gentlemen, distinguished members of the Bar and Bench—including the laboratory bench—I have a document to prove that Dr. Amos has allowed me these 10 minutes and, like a commercial radio sponsor, I intend to use every second of them.

"I had the opportunity on a flight back from Paris yesterday to read the manuscripts of the papers you heard this afternoon, and during the wee hours of the morning I dashed off my remarks. I hope you will forgive me if I read them. I would add that they are in my own handwriting and they may be a bit difficult to decipher.

"The addresses we have heard this morning and this afternoon illustrate that the impact of the present chemical age has been felt with considerable force not only by the food industry but by the legal profession as well. Doctors Thatcher and Morrell have emphasised the highly technical nature—and you will understand this better when you see their manuscripts in print—of the questions that must be considered in arriving at a judgement permitting the use of antibiotics as food preservatives. In fact similar criteria must be employed in evaluating the safety of any kind of food additives. Antibiotics are simply a special case of the ever-broadening general class of preservatives which include not only these biological products, but chemical, antimicrobial agents, antioxidants and chelating compounds, and also such treatments as atomic or nuclear radiation.

"That food preservation is a vital part of modern industrial science is evident from the fact that foods are seldom eaten at the site or at the time of production. They must be packed, transported and stored. It is no longer a question of whether food shall be preserved, but how best to accomplish this. The retention of nutritional qualities and consumer acceptability are, of course, a sine qua non, but safety must not be sacrificed to these ends.

"This paper seeks to illustrate the wide variety of disciplines, or rather specialties within specialties, that must be called upon for a proper assessment of problems relating to the use of new food additives. The chemist who makes the substances needs the agronomist or food technologist to establish their utility. Then the toxicologist needs specialists in pathology, allergy or oncology to aid in laying the experimental foundation for the appraisal of safety. Statisticians play a significant role in the interpretation of the scientific data and, ultimately, judgments must be rendered which take all factors into account, weighing benefits, however great they may be, against risks, however slight.

"At this point it must be said that the hazards attending the use of food additives (whether antibiotics, emulsifiers,

antioxidants, flavourings and colouring agents, or any of the other categories mentioned by Dr. Welch) are frequently exaggerated out of all proportion to their real dimensions. No chemical intentionally added to foods in the course of normal production presents anywhere near as great a risk to the consumer as does the use of tobacco or alcohol. This is not to say that caution must be thrown to the winds. Effective governmental control is necessary, but we should appreciate that the food manufacturer has little to gain by subjecting his customers to jeopardy. His competitors would soon take care of him if the enforcement agencies did not.

"As Mr. Bacharach has so ably pointed out, much of the evidence relating to antibiotics in foods is new. The prospects of usefulness are extremely great, particularly in those areas where refrigeration is scarce and high protein foods are needed. The hazards are recognised, but present evidence indicates that they are slight, if indeed they exist at all.

"Doctors Thatcher and Morrell have stated that antibiotics are of little use where sanitary conditions are poor, so the possibility of their leading to unhygienic conditions in food plants is virtually non-existent. In fact, experience is showing the contrary to be the case, and that improved sanitation develops where antibiotics are in use.

"Laws need to be tightened up, however, so that any possible injury is prevented rather than punishing the offender after the injury has been done. Suitable and workable legislation should be developed in an atmosphere of calm deliberation. Despite the apprehensions and alarms blared forth in the lay press the fact is that no real or imminent danger is known to exist. The cry of 'Cancer!' is based not on experimental evidence but on often unsupported suspicion and speculation.

"Consumers could well recall the words of a great American uttered in another context, that the only thing we have to fear is fear itself. Some have the impression that carcinogenic potentialities of chemical substances are readily detected experimentally, but that a negligent or economy-minded industry would prefer not to look where danger lurks. That is entirely unfounded. The fact is that there is substantial disagreement as to what is meant by a dietary carcinogen. The differences in susceptibility between animal species, the differences even within species due to route of administration or the amount and duration of dosage, the effects of variations in experimental diets, the incidence of tumour growths in 'normal' laboratory animals, all of these combine to make it exceedingly difficult, if not impossible, to say unequivocally of any substance that its consumption by man under normal conditions of use is attended with no possible risk of cancer. And if the experiments were limited to a single species, like the rat, and only to oral dosage, the results, if negative, would be even less conclusive.

"All of which calls for a rational approach to the question of safety in use of the growing list of additives of value in preserving and expanding our food supply. As Dr. Welch has so clearly put it, when speaking of antibiotics in the treatment of bovine mastitis, education is required in the proper use of additives. There is likewise great need to educate consumers as to the advantages and benefits that accrue to them through more nutritious, more appealing, better keeping, more convenient and more varied foods. Labelling may play a greater role not only in apprising the consumer of the reasons for additives but, in special cases, to protect the unusually sensitive, as in the case of penicillin-containing milk. (It may be noted in passing, however, that a law which defines foods in terms of their mandatory and optional ingredients, but which does not require these to be declared on the label, offers little

protection to the hypersensitive or allergic consumer.)

"The possibility of expanding uses of chemicals in general and of antibiotics in particular poses many questions to the scientist, the lawyer and the public health official alike. Some involve matters of public policy such as whether the control officials should be permitted to pass on the utility of additives, or whether a safety valve should be provided to protect industry against overzealousness on the part of administrative officials. But let it not be considered that scientific determinations upon which the assessment of safety so largely depends is not without its quota of subjective judgement in both the planning and the interpretation of experiments.

"The CHAIRMAN: I will now call upon Dr. Ingram.

"Dr. M. INGRAM: I wish, sir, in effect to ask a question about the paper or printed matter of Morrell and Thatcher. Therein they listed a number of criteria which were determining whether antibiotics are suitable for use.

"The fifth of these criteria, if I have it rightly, was that the antibiotics should induce no abnormal spoilage pattern. This requirement I observe is ranked above that that there should be complete destruction of the antibiotics on cooking, the importance of which was plain from what Mr. Harvey said this morning.

"This question of the spoilage pattern is one of which I have had some experience, and I wonder whether I might venture the assertion that there is no case in which the use of an antibiotic does not result in an abnormal spoilage pattern. What is more, in the two particular cases, those of the use of chlortetracycline in poultry and fish, which have already been legalised in America, the scientific evidence is perfectly plain and unambiguous that the spoilage pattern is abnormal, the normal bacterial spoilage flora being released by one of the algae. There is no published evidence known to me which will tell us what kind of algae they are. It seems to be assumed that all these are automatically harmless. That is not quite true. It seems to me therefore that this criterion is more honoured in the breach than in the observance, and I should be very grateful to hear just a little more of what exactly it amounts to.

"The CHAIRMAN: In the absence of the authors of the paper, unless Dr. Wright or Mr. Harvey wish to comment, we will take a note of the question and refer it to the authors.

"Does anyone else wish to take part in this discussion?

"Mr. A. L. BACHARACH: Might I add a supplementary to Dr. Ingram's question—whether there is any preservative whatsoever that does not alter the spoilage pattern?

"The CHAIRMAN: I think that, Mr. Bacharach, is a very reasonable question.

"I feel sure now that our Chairman of this morning should be given an opportunity, if he wishes, to address us again. We are so delighted to have him here. Mr. Dunn, would you care to come forward?

"Mr. Charles Wesley DUNN: Mr. Chairman, ladies and gentlemen, I have only a few words to say. I would like to say first on behalf of the Institute of the United States, our distinguished guests and other friends here from across the Atlantic, how deeply we appreciate your hospitality on this most distinguished and valuable educational occasion, and we are especially grateful to the committee which worked so hard to organise this meeting which involved so many details and problems to be solved. The committee consisted of Dr. Amos, Dr. Adams, Dr. Voelcker, Mr. Charles Adams and Dr. Kent Jones.

"A special reference should be made to Dr. Amos. He has worked indefatigably for the success of this conference, and it has been a very great success. We would be wanting in courtesy and in appreciation if we did not record our deep gratitude to Dr. Amos for all he has done.

"The second and concluding statement that I would like to make is that I am one of those individuals who believes that all human progress comes about through human association and common discussion of common problems, and therefore we on the part of the Food Law Institute of the United States would like to suggest to our three distinguished scientific collaborators or sponsors of this conference that we set up a skeleton organisation to renew this sort of a conference that we have had here today in the future, and I hope it will not be too long again in the future. We would be quite happy to have the conference again right here in London, and we will guarantee to bring over to you by one means or another our United States and Canadian Commissioners of Food and Drugs and our leaders also like our distinguished friend here from New York today, to join in this conference. Therefore I hope that you will approve of this suggestion that we have tried to use this occasion not to lose what we have gained, but to continue it. I thank you.

"The CHAIRMAN: Ladies and gentlemen, you will wish me to say that it has been just as much of an honour to receive our guests. I myself have had no part whatsoever in the organisation of this conference, but one thing has struck me about it, and that is the great virtue which comes from the opportunity which it afforded for an exchange of views. It has been the first occasion which I can remember upon which representatives—and I wish there had been more of them—of those who are responsible for safeguarding public health have been present, or have been represented by papers at any rate, in this country. The problems with which those authorities, be it in the United States, Canada or in this country, have to face in respect of these new substances with which we are concerned, are common problems. The method of solution of those problems may well be a little different in each of those countries, but I am convinced that a discussion of those problems, the bringing together of our united information regarding them, and you never get that by relying upon publications—you have to get together the people who are dealing with the problems—because no-one commits himself to paper until he has a cast-iron case and it will be a long time before we shall have a cast-iron case here—will give us a lot of valuable information and experience which is available in all these authorities which, I am convinced, it will be worth while bringing together. The problem is how we can bring them together, except on the occasion of meetings of which I would consider this just the first, or what I might call a more formal opening, and let us hope that we shall get people freely expressing their views, and not necessarily the views that we publish, in order to stimulate thought and expression of opinions from others who are concerned with the same problems and the same field.

"Please do not think for one moment that I am suggesting that the food and drug laws in this country should necessarily be an exact copy of those in the United States or Canada. Conditions are different, our methods of enforcing them are different; they call for a different approach, but I would say again the problem we have to face is the same. Let us at least hear all the information we can concerning those problems so that we can find the best and most useful answer.

"And now, Dr. Voelcker, I would ask you to comment.

"Dr. Eric VOELCKER: . . .

"I was more than honoured when I was asked to say a few words to thank the writers of the papers for all the time and thought given to the subject, and all those who contributed to the discussion both this morning and this afternoon. I feel that we have suffered greatly by the absence of Mr. Larrick, Dr. Lehman, Dr. Welch, Dr. Morrell and Dr. Thatcher, but we are indeed fortunate that Dr. Harvey, Dr. Oser and Mr. Adams have so kindly con-

sented to read their papers for them—a most unenviable task and one which I think we must all agree was admirably accomplished. Rarely have I listened to seven more interesting papers, papers that when we have a reprint will become, I feel absolutely sure, a priceless possession to all of us in this particular field of work.

"The discussion too has shown that a very keen interest has been taken in this question of additives to food, and we are indeed fortunate in having so many scientists here today not only from various parts of this country but from America and Europe.

"We are fortunate, too, in our two Chairmen today, Mr. Charles Wesley Dunn and Sir Harry Jephcott. I cannot think of a better choice, and we are all indeed indebted to them for seeing that the two meetings have been conducted in a fit and orderly manner.

"Mr. Charles Wesley Dunn has stolen my thunder a little now, because I was going to mention Dr. Amos, and this is what I was going to say. There is one name that does not appear in the list as a speaker, nor has he said anything in the discussion, but without him this meeting would not have been the success that it undoubtedly has been. That gentlemen is Dr. Amos. He has worked like no other man would or could, and I should be lacking in my duty if I were not to mention to you how deeply we are in his debt for all that he has done.

"Now, ladies and gentlemen, I would ask you all to show your appreciation and thanks to all who have helped to make these two meetings such a success, in the accustomed manner.

"(Applause.)

"The CHAIRMAN: Before concluding the meeting I think there is one request you would wish me to make to Dr. Amos, although it is adding a little more to his job, and that is that he will express on behalf of all of us—the meeting as a whole—our deep indebtedness to those who have sent their papers but were unable to be with us, and say how deeply we regret that they are not here. I think that they should know.

"Thank you, ladies and gentlemen, that terminates the business of this conference."

Statement on Conference — *The Times*, July 26, 1957.—The following statement appeared on the editorial page of *The* [*London*] *Times*, for July 26:

"THE SCIENTIST AT TABLE

"USE OF CHEMICALS IN FOOD

"By A. L. Bacharach

"I write as a food chemist. Man has almost certainly never had enough to eat. What is characteristic of our own age is that we are not only conscious of the wide, and ever growing, gap between the world's food requirements and the world production of crops and stock, but that we are also increasingly anxious to do something about it. To this end greater food production is the direct and most obvious means. But there are other means and, in the aggregate, they might make an impressive contribution towards abolishing the under-nutrition, and sometimes even the frank starvation that are a direct result of to-day's adverse food balance.

"The total prevention of wastage among growing or stored animal and vegetable produce—wastage due to a vast variety of animal and vegetable predators—would, it has been calculated, give the world 10 per cent more food. Here is a subject highly suitable for discussion on an international basis. That is why results of interest and value may be hoped for from the meeting at the Royal Institution, to-day, between American food lawyers and British food technologists and public analysts. They are to discuss some of the practical and theoretical issues arising on both sides of the Atlantic. Canadian procedures in this field are nearer those of the United States than those of Great Britain.

"FIT FOR ANIMALS

"Judicious application of knowledge already possessed by food technologists could make many foods more palatable. Among them there are certainly some that have a present too low a 'consumer acceptance' to be fit for anything but feeding to stock animals at best. The need for greater economy in the use of available food supplies is widely recognized by medical and scientific authorities and by democratic legislatures. This is certainly one reason why the description 'chemicals in food' is no longer necessarily a term of abuse, applied to something primarily used to swell the profits of manufacturers in the food and chemical industries.

"There are two substantially distinct routes by which substances added to foodstuffs to preserve them or to improve their taste may come to be present in food as eaten. They may have been added to flavour, to colour, or to preserve the food, or to increase its nutritive value. Such substances are intended to remain in the food right up to, or at, the time when it is to be consumed. Alternatively, they may be present as the result of some treatment during growing or processing, though not wanted in the finished product.

"Thus, an insecticide may have been used to clean up stored grain, a fungicide to protect a growing crop of vegetables, or an antibiotic to supplement the feedingstuff of a young chick or pig. Although traces of such substances may remain in the final food, this is the exception, as they have usually been converted to harmless breakdown products, in the treated plant or animal, or been removed during subsequent stages of processing. In other cases they are destroyed by exposure to atmospheric oxygen or by the digestive ferments of the consumer.

"OFFICIAL CHECKS

"Nevertheless it is entirely right that public attention, particularly that of governmental and medical authorities, should be kept focused on the problem and that any new practice involving the presence in food of what are technically known as 'additives' should be permitted only after thorough investigation has established three things. First, it must have been shown that the proposed use is capable of producing a real improvement in food production, storage or consumption. Secondly, it must have been demonstrated by the best available techniques that the quantities present or persisting in the food as eaten must be such as are unlikely to cause any kind of harm to the consumer, no matter how much of the food he may eat.

"Some authorities particularly emphasize what all food scientists would accept: that there is a difference in kind, and not merely in degree, between substances that are simple poisons and those capable of producing malignant tumours. The effects of the former are reversible if detected and dealt with in time. Those of the latter are almost certainly self-perpetuating and will continue unchecked, especially if unrecognized, after the cancer stimulus has been completely withdrawn.

"HOW TO MEASURE

"A third condition that must attach to the use of a food-processing agent, or 'additive', is that there are valid and practicable analytical procedures for measuring, with the necessary degree of accuracy, the amounts likely to be present in any food in which it may occur. Particularly is this essential when the amounts are close to whatever limits have been permitted by legal enactment or accepted responsible industrial practice. This condition tends sometimes to be overlooked by legislators and administrators who do not properly appreciate the special analytical problems that inevitably arise in the examination of such complex mixtures as human foods of animal or vegetable origin.

"Food and drug authorities of the British Commonwealth and the United States of America, as well as the other western democracies, are fully conversant with the benefits that can legitimately be claimed, from the skilled

use under proper control of suitable 'chemicals in food'. At the same time they are fully appreciative of the risks to human health and the means available for reducing those risks to a minimum. It is now virtually universal practice in these countries to forbid the use of any additive (for any agent leaving a residue) unless it can be said with a high degree of probability that the quantities remaining in the treated food can be detected and are harmless. It is not even enough that they shall not have been shown to be harmful. A verdict of 'not proven' harmless will generally be sufficient to exclude from a country's 'permitted list' of food colours, flavouring agents, antioxidants, emulsifiers, processing aids, antibotics or pesticides—to mention only the main categories of such preparations used in the food industry.

"IMPROVING TASTE

"Not unreasonably, the chemical manufacturer wishes to secure the widest possible sales for new substances elaborated by his research staff. The food manufacturer is just as anxious, and with as much reason, to use every modern aid for increasing the stability, acceptability, and nutritive value of his products. (In this connexion it is relevant to note that the addition of vitamins A and D to margarine and of vitamin B to bread, legally mandatory in this country and the United States of America, is in the strictest sense the addition of 'chemicals' to food.) Yet it is not, as has sometimes been glibly and incorrectly alleged, the job of the food technologist to aid and abet each and every scheme for adding as many chemicals to as many foods as possible.

"On the contrary, the whole of his instincts, training and knowledge—the latter necessarily including something more than a merely nodding acquaintance with nutrition, biochemistry, physiology, pharmacology, toxicology, and bacteriology—is against adding anything whatever to food if the desired end can be reached without it.

"For every occasion on which he advises his company that some process involving the use of an 'aduitive' or the presence of a residue is permissible, there will be a dozen times or more when he will feel obliged to play the role—far from Mephistophelian in this instance—of 'the spirit that always denies'.

"The food technologist is aided by and usually works in the closest harmony with, national and local public health authorities and medical and other scientists engaged in biological research. With them he has a primary duty to see to it that processes involving the appearance of 'additives' and residues in our food are only used when undoubted benefit should accrue from them and when the risks from their presence are so small as to be virtually non-existent."

Attendance at Conference.—Attendance at the conference sessions exceeded 400. Delegates came from throughout England, Scotland and Wales, from the United States and from numerous Western European countries.

An evening dinner was also held, given by the participating British societies, in honor of The Food Law Institute. The Honorable Justice Lloyd-Jacob served as chairman of the dinner, with an attendance of more than 100.

Plans for Future Meetings.—Mr. Dunn has announced that it was decided at the conference to continue the valuable international discussion of food problems, for educational purposes. The time of the next conference has not, however, been finally established. It was further decided to have another meeting at London in 1960, to commemorate the centennial anniversary of England's national pure-food law, the first such measure enacted in the English-speaking world. According to Mr. Dunn's announcement, The Food Law Institute will arrange for government, industry and scientific delegates from the United States.

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